

This is a repository copy of *Antipsychotics for treatment of delirium in hospitalised non-ICU patients*.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/132847/>

Version: Published Version

---

**Article:**

Burry, Lisa, Mehta, S.R., Perreault, M.M et al. (6 more authors) (2018) Antipsychotics for treatment of delirium in hospitalised non-ICU patients. Cochrane Database of Systematic Reviews. CD005594. ISSN 1469-493X

<https://doi.org/10.1002/14651858.CD005594.pub3>

---

**Reuse**

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

**Takedown**

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing [eprints@whiterose.ac.uk](mailto:eprints@whiterose.ac.uk) including the URL of the record and the reason for the withdrawal request.



**Cochrane**  
**Library**

**Cochrane** Database of Systematic Reviews

## **Antipsychotics for treatment of delirium in hospitalised non-ICU patients (Review)**

Burry L, Mehta S, Perreault MM, Luxenberg JS, Siddiqi N, Hutton B, Fergusson DA, Bell C, Rose L

Burry L, Mehta S, Perreault MM, Luxenberg JS, Siddiqi N, Hutton B, Fergusson DA, Bell C, Rose L.

Antipsychotics for treatment of delirium in hospitalised non-ICU patients.

*Cochrane Database of Systematic Reviews* 2018, Issue 6. Art. No.: CD005594.

DOI: 10.1002/14651858.CD005594.pub3.

**[www.cochranelibrary.com](http://www.cochranelibrary.com)**

## TABLE OF CONTENTS

HEADER . . . . .	1
ABSTRACT . . . . .	1
PLAIN LANGUAGE SUMMARY . . . . .	2
SUMMARY OF FINDINGS FOR THE MAIN COMPARISON . . . . .	4
BACKGROUND . . . . .	7
OBJECTIVES . . . . .	8
METHODS . . . . .	8
RESULTS . . . . .	11
Figure 1. . . . .	12
Figure 2. . . . .	14
Figure 3. . . . .	15
Figure 4. . . . .	17
Figure 5. . . . .	18
Figure 6. . . . .	19
Figure 7. . . . .	19
Figure 8. . . . .	20
Figure 9. . . . .	20
Figure 10. . . . .	21
Figure 11. . . . .	22
ADDITIONAL SUMMARY OF FINDINGS . . . . .	22
DISCUSSION . . . . .	26
AUTHORS' CONCLUSIONS . . . . .	27
ACKNOWLEDGEMENTS . . . . .	27
REFERENCES . . . . .	28
CHARACTERISTICS OF STUDIES . . . . .	34
DATA AND ANALYSES . . . . .	54
Analysis 1.1. Comparison 1 Severity of delirium, Outcome 1 Antipsychotic versus no antipsychotic. . . . .	55
Analysis 1.2. Comparison 1 Severity of delirium, Outcome 2 Sensitivity analysis (placebo-controlled studies only). . . . .	56
Analysis 1.3. Comparison 1 Severity of delirium, Outcome 3 Sensitivity analysis (trials at low risk of bias). . . . .	56
Analysis 1.4. Comparison 1 Severity of delirium, Outcome 4 Typical versus atypical antipsychotic. . . . .	57
Analysis 2.1. Comparison 2 Resolution, Outcome 1 Antipsychotic versus no antipsychotic. . . . .	58
Analysis 2.2. Comparison 2 Resolution, Outcome 2 Sensitivity analysis (including placebo studies). . . . .	58
Analysis 2.3. Comparison 2 Resolution, Outcome 3 Resolution (atypical versus typical antipsychotic). . . . .	59
Analysis 3.1. Comparison 3 Mortality, Outcome 1 Mortality (antipsychotic versus no antipsychotic). . . . .	60
Analysis 3.2. Comparison 3 Mortality, Outcome 2 Sensitivity analysis (including only placebo studies). . . . .	60
Analysis 3.3. Comparison 3 Mortality, Outcome 3 Mortality (atypical versus typical antipsychotic). . . . .	61
Analysis 4.1. Comparison 4 Adverse Event, Outcome 1 Antipsychotic versus no antipsychotic (EPS). . . . .	62
Analysis 4.2. Comparison 4 Adverse Event, Outcome 2 Typical versus atypical antipsychotic (EPS). . . . .	62
APPENDICES . . . . .	63
WHAT'S NEW . . . . .	108
HISTORY . . . . .	109
CONTRIBUTIONS OF AUTHORS . . . . .	109
DECLARATIONS OF INTEREST . . . . .	109
SOURCES OF SUPPORT . . . . .	109
DIFFERENCES BETWEEN PROTOCOL AND REVIEW . . . . .	110
INDEX TERMS . . . . .	110

# Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Lisa Burry<sup>1</sup>, Sangeeta Mehta<sup>2</sup>, Marc M Perreault<sup>3</sup>, Jay S Luxenberg<sup>4</sup>, Najma Siddiqi<sup>5</sup>, Brian Hutton<sup>6</sup>, Dean A Fergusson<sup>7</sup>, Chaim Bell<sup>8</sup>, Louise Rose<sup>9</sup>

<sup>1</sup>Department of Pharmacy, Mount Sinai Hospital, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Canada. <sup>2</sup>Interdepartmental Division of Critical Care Medicine, Mount Sinai Hospital, University of Toronto, Toronto, Canada. <sup>3</sup>Faculty of Pharmacy, Université de Montréal, Montreal, Canada. <sup>4</sup>On Lok, San Francisco, California, USA. <sup>5</sup>Department of Health Sciences, Hull York Medical School, University of York, York, UK. <sup>6</sup>Knowledge Synthesis Group, Ottawa Hospital Research Institute, Ottawa, Canada. <sup>7</sup>Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Canada. <sup>8</sup>Medicine, Mount Sinai Hospital, Toronto, Canada. <sup>9</sup>Department of Critical Care Medicine, Sunnybrook Health Sciences Centre and Sunnybrook Research Institute, Toronto, Canada

Contact address: Lisa Burry, Department of Pharmacy, Mount Sinai Hospital, Leslie Dan Faculty of Pharmacy, University of Toronto, 600 University Avenue, Room 18-377, Toronto, ON, M5G 1X5, Canada. [lisa.burry@sinaihealthsystem.ca](mailto:lisa.burry@sinaihealthsystem.ca).

**Editorial group:** Cochrane Dementia and Cognitive Improvement Group.

**Publication status and date:** New search for studies and content updated (conclusions changed), published in Issue 6, 2018.

**Citation:** Burry L, Mehta S, Perreault MM, Luxenberg JS, Siddiqi N, Hutton B, Fergusson DA, Bell C, Rose L. Antipsychotics for treatment of delirium in hospitalised non-ICU patients. *Cochrane Database of Systematic Reviews* 2018, Issue 6. Art. No.: CD005594. DOI: 10.1002/14651858.CD005594.pub3.

Copyright © 2018 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

## ABSTRACT

### Background

Guidelines suggest limited and cautious use of antipsychotics for treatment of delirium where nonpharmacological interventions have failed and symptoms remain distressing or dangerous, or both. It is unclear how well these recommendations are supported by current evidence.

### Objectives

Our primary objective was to assess the efficacy of antipsychotics versus nonantipsychotics or placebo on the duration of delirium in hospitalised adults. Our secondary objectives were to compare the efficacy of: 1) antipsychotics versus nonantipsychotics or placebo on delirium severity and resolution, mortality, hospital length of stay, discharge disposition, health-related quality of life, and adverse effects; and 2) atypical vs. typical antipsychotics for reducing delirium duration, severity, and resolution, hospital mortality and length of stay, discharge disposition, health-related quality of life, and adverse effects.

### Search methods

We searched MEDLINE, Embase, Cochrane EBM Reviews, CINAHL, Thomson Reuters Web of Science and the Latin American and Caribbean Health Sciences Literature (LILACS) from their respective inception dates until July 2017. We also searched the Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment Database, Web of Science ISI Proceedings, and other grey literature.

### Selection criteria

We included randomised and quasi-randomised trials comparing 1) antipsychotics to nonantipsychotics or placebo and 2) typical to atypical antipsychotics for the treatment of delirium in adult hospitalised (but not critically ill) patients.

## Data collection and analysis

We examined titles and abstracts of identified studies to determine eligibility. We extracted data independently in duplicate. Disagreements were settled by further discussion and consensus. We used risk ratios (RR) with 95% confidence intervals (CI) as a measure of treatment effect for dichotomous outcomes, and between-group standardised mean differences (SMD) with 95% CI for continuous outcomes.

## Main results

We included nine trials that recruited 727 participants. Four of the nine trials included a comparison of an antipsychotic to a nonantipsychotic drug or placebo and seven included a comparison of a typical to an atypical antipsychotic. The study populations included hospitalised medical, surgical, and palliative patients.

No trial reported on duration of delirium. Antipsychotic treatment did not reduce delirium severity compared to nonantipsychotic drugs (standard mean difference (SMD) -1.08, 95% CI -2.55 to 0.39; four studies; 494 participants; very low-quality evidence); nor was there a difference between typical and atypical antipsychotics (SMD -0.17, 95% CI -0.37 to 0.02; seven studies; 542 participants; low-quality evidence). There was no evidence antipsychotics resolved delirium symptoms compared to nonantipsychotic drug regimens (RR 0.95, 95% CI 0.30 to 2.98; three studies; 247 participants; very low-quality evidence); nor was there a difference between typical and atypical antipsychotics (RR 1.10, 95% CI 0.79 to 1.52; five studies; 349 participants; low-quality evidence). The pooled results indicated that antipsychotics did not alter mortality compared to nonantipsychotic regimens (RR 1.29, 95% CI 0.73 to 2.27; three studies; 319 participants; low-quality evidence) nor was there a difference between typical and atypical antipsychotics (RR 1.71, 95% CI 0.82 to 3.35; four studies; 342 participants; low-quality evidence).

No trial reported on hospital length of stay, hospital discharge disposition, or health-related quality of life. Adverse event reporting was limited and measured with inconsistent methods; in those reporting events, the number of events were low. No trial reported on physical restraint use, long-term cognitive outcomes, cerebrovascular events, or QTc prolongation (i.e. increased time in the heart's electrical cycle). Only one trial reported on arrhythmias and seizures, with no difference between typical or atypical antipsychotics. We found antipsychotics did not have a higher risk of extrapyramidal symptoms (EPS) compared to nonantipsychotic drugs (RR 1.70, 95% CI 0.04 to 65.57; three studies; 247 participants; very-low quality evidence); pooled results showed no increased risk of EPS with typical antipsychotics compared to atypical antipsychotics (RR 12.16, 95% CI 0.55 to 269.52; two studies; 198 participants; very low-quality evidence).

## Authors' conclusions

There were no reported data to determine whether antipsychotics altered the duration of delirium, length of hospital stay, discharge disposition, or health-related quality of life as studies did not report on these outcomes. From the poor quality data available, we found antipsychotics did not reduce delirium severity, resolve symptoms, or alter mortality. Adverse effects were poorly or rarely reported in the trials. Extrapyramidal symptoms were not more frequent with antipsychotics compared to nonantipsychotic drug regimens, and no different for typical compared to atypical antipsychotics.

## PLAIN LANGUAGE SUMMARY

### Antipsychotics to treat delirium in hospitalised patients, not including those in intensive care units

#### Review question

We reviewed the evidence for the effectiveness and safety of antipsychotics for treatment of delirium in hospitalised patients, not including those in intensive care units (specialised wards for caring for very sick patients).

#### Background

Delirium is a public health concern as it is a new onset confused state that increases the amount of time patients spend in the hospital, as well as their chance of dying. Guidelines recommendations include reversal of any potential medical or drug triggers that may be contributing to delirium. If delirium symptoms persist and are distressing or dangerous, an antipsychotic drug may be prescribed for a short time. Antipsychotic drugs, also known as tranquillizers, are mainly used to treat psychosis (e.g. hallucinations). There are two types of antipsychotics: first generation or typical antipsychotics (e.g. haloperidol) and second generation or atypical antipsychotics (e.g. quetiapine). Both groups of antipsychotics block the brain's dopamine receptor pathways but atypical antipsychotics also act on

serotonin receptors. Atypical antipsychotics are also noted to be effective for treating both the positive symptoms (e.g. hallucinations) as well as the negative symptoms (e.g. emotional withdrawal) of psychosis. We need to understand if antipsychotics shorten the course of delirium or reduce symptoms or if they cause more harm. Therefore, we updated the existing Cochrane Review from 2007.

### **Study characteristics**

We found nine studies with 727 participants testing antipsychotics for delirium treatment; four trials compared an antipsychotic to another drug class or placebo and seven of the nine trials compared a typical antipsychotic to an atypical antipsychotic.

### **Key findings**

We found no evidence to support or refute the suggestion that antipsychotics shorten the course of delirium in hospitalised patients. Based on the available studies, antipsychotics do not reduce the severity of delirium or resolve symptoms compared to nonantipsychotic drugs or placebo or lower the risk of dying. We found no evidence to support or refute the suggestion that antipsychotics shorten hospital length of stay or improve health-related quality of life. Side effects were rarely reported in the studies.

### **Quality of the Evidence**

It is important to note many clinically relevant outcomes were not reported in the studies and the overall quality of the available evidence was poor.

### **External funding**

Canadian Frailty Network (previously Technology Evaluation in the Elderly Network [TVN]) ([www.cfn-nce.ca/](http://www.cfn-nce.ca/)), Canada

## SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Antipsychotics for the treatment of delirium in hospitalised patients						
<b>Patient or population:</b> delirious patients <b>Settings:</b> hospital wards, not ICU <b>Intervention:</b> antipsychotics drugs <b>Comparison:</b> nonantipsychotics drugs or placebo						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Non-antipsychotics drugs or Placebo	Antipsychotics drugs				
<b>Duration of delirium</b> Follow-up: days						This outcome was not reported in any trial.
<b>Delirium severity</b> DRS, DRS-R98, MDAS <sup>1</sup> Follow-up: up to 10 days	The mean DRS-R98 score was 22.7 (3.1) at baseline and 7.4 (SD 3.3) at the end of study. <sup>16</sup>	The standardised delirium severity score was <b>1.08 points lower</b> in the intervention group (2.55 lower to 0.39 higher).		494 (4 studies)	⊕○○○ <b>Very low-quality:</b> we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect. 2,3,4,5	SMD -1.08 (-2.55 to 0.39)
<b>Delirium resolution</b> DRS, DRS-R98 <sup>1</sup> Follow-up: up to 10 days	<b>Study population</b>		<b>RR 0.95</b> (0.3 to 2.98)	247 (3 studies)	⊕○○○ <b>Very low-quality:</b> we have very little confidence in the effect estimate; the true effect is likely to be substantially different from	

				the estimate of effect. 6,7,8,9,10
	268 per 1000	254 per 1000 (80 to 798)		
	Moderate			
	191 per 1000	181 per 1000 (57 to 569)		
<b>Mortality</b> Follow-up: up to 10 days	Study population		RR 1.29 (0.73 to 2.27)	319 (3 studies)
	126 per 1000	163 per 1000 (92 to 286)		⊕⊕○○ <b>Low-quality:</b> we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different. <sup>11,12</sup>
	Moderate			
	143 per 1000	184 per 1000 (104 to 325)		
<b>Hospital length of stay</b> Follow-up: days				This outcome was not reported in any trial.
<b>Adverse Effects - EPS</b> Extrapyramidal Symptom Rating Scale, or not reported Follow-up: up to 10 days	Study population		RR 1.7 (0.04 to 65.57)	247 (3 studies)
	54 per 1000	91 per 1000 (2 to 1000)		⊕○○○ <b>Very low-quality:</b> we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect. 13,14,15
	Moderate			
	0 per 1000	0 per 1000 (0 to 0)		



\*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**CI:** Confidence interval; **DRS:** Delirium Rating Scale; **DRS-R98** = Delirium Rating Scale Revised 98; **EPS:** Extrapyramidal Symptoms; **MDAS:** Memorial Delirium Assessment Scale; **RR:** Risk ratio; **SD:** standard deviation

GRADE Working Group grades of evidence

**High quality:** Further research is very unlikely to change our confidence in the estimate of effect.

**Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

**Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low quality:** We are very uncertain about the estimate.

<sup>1</sup> DRS = Delirium Rating Scale; DRS-R98 = Delirium Rating Scale -Revised 98; MDAS = Memorial Delirium Assessment Scale

<sup>2</sup> Only 1 of the 4 trials was considered low risk of bias across all domains. Three of the four trials had blinded delirium assessment.

<sup>3</sup> Very high heterogeneity (97%).

<sup>4</sup> Delirium severity was measured with different tools at variable time points.

<sup>5</sup> Wide confidence interval that included both no effect and benefit.

<sup>6</sup> All included trials had risk of bias.

<sup>7</sup> Blinded delirium assessment for two of the three trials.

<sup>8</sup> High degree of heterogeneity (83%)

<sup>9</sup> Delirium resolution was measured with different tools at variable time points using different thresholds.

<sup>10</sup> Wide confidence interval.

<sup>11</sup> Only 1 trial had low risk of bias across all domains.

<sup>12</sup> Low number of events.

<sup>13</sup> All trials at risk of bias.

<sup>14</sup> Variable tools used to assess.

<sup>15</sup> Few events and wide confidence intervals.

<sup>16</sup> Assumed risk taken from [Tahir 2010](#).

## BACKGROUND

### Description of the condition

Delirium is a dangerous and common syndrome among hospitalised patients (Inouye 2006a). It is estimated to be present in 8% to 17% of all older patients in the emergency department, and 29% to 64% of general medical and older adult inpatients (Inouye 2014). Delirium is most prevalent in frail individuals such as those with pre-existing cognitive impairments (e.g. dementia), having undergone surgery, or suffering an acute infection or critical illness (Inouye 2014; Rudolph 2011; Salluh 2010).

The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) of the American Psychiatric Association defines delirium as a complex syndrome characterised by disturbances in attention (i.e. ability to focus, sustain or shift attention), awareness (i.e. orientation), and cognition (i.e. memory, perception) not explained by a pre-existing neurocognitive disorder (DSM-V 2013). Unlike dementia, the onset of delirium is rapid (i.e. over the course of hours or days); symptoms fluctuate and are typically reversible. The symptoms of delirium are unpredictable and irregular, contributing to its under-detection (Inouye 2001). Based on the predominance of type of psychomotor symptoms, delirium is categorized as hyperactive, hypoactive, or mixed (i.e. presenting with periods of both hyper- and hypoactivity) (Cole 2009).

The cause of delirium is thought to be multifactorial, dependent on a complex interplay of predisposing and precipitating factors (i.e. environment and iatrogenic (i.e. caused by medical examination or treatment) (Gleason 2003; Rolfson 2002), and mitigated or aggravated by a cascade of physiological events yet to be fully characterised. Predisposing risk factors are numerous and include advanced age, smoking and alcohol abuse, severe illness, and the presence of medical comorbidities such as hypertension and dementia (Gleason 2003; Inouye 1996; Inouye 2014; Rolfson 2002; Vasilevskis 2012). Patients with multiple risk factors appear to be sensitive to even minor precipitating insults, whereas those without such risk factors may develop delirium only following a major insult (e.g. sepsis). While the definitive cause of delirium is unknown, evidence suggests several biological networks may interact to cause the syndrome (Watt 2013). Postulated mechanisms include genetic factors, physiological stressors (e.g. inflammation, increased metabolism, decreased oxygenation, electrolyte imbalances), and disruptions in neurotransmitters involved in cognitive function (Cerejeira 2010; Inouye 2014). Several neurotransmitter systems have been implicated (Gaudreau 2005), but a relative acetylcholine deficiency and/or dopamine excess are most supported by current literature (Flacker 1999; Hsieh 2008; MacLulich 2013; Trzepacz 1999; Trzepacz 2000; Young 1997; ).

### Description of the intervention

Current professional society guidelines direct the diagnosis, prevention, and management of delirium for patients in various hospital settings (Barr 2013; British Geriatric Society 2006; NICE 2010; RCP 2006). The recommended first steps in delirium care involve identifying and reversing potential precipitating medical conditions, mitigating environmental triggers, and minimising drug exposures. Different combinations of strategies have been used and include resolving acute medical issues, managing pain, applying reorientation strategies, normalising the sleep-wake cycle, ensuring safe mobilisation, and evaluating potential drug-related causes (Fosnight 2011; Inouye 2006b; Inouye 2014; Lundstrom 2005). Numerous classes of psychoactive drugs (e.g. antipsychotics, benzodiazepines, opioids, alpha-2 agonists, and cholinesterase inhibitors) have been studied for their effect on delirium in various patient populations. However, data are inconsistent and practice remains largely governed by clinical circumstance and physician discretion. Because of the uncertainty surrounding antipsychotic effectiveness in delirium, professional societies recommend limited and cautious use, and only in cases where nonpharmacological approaches have failed and symptoms remain distressing or dangerous, or both, to the patient or healthcare staff, or both (American Psychiatric Association 1999; CEHSE 2006; NICE 2010).

Antipsychotic drug exposure is associated with notable risk that should be considering when prescribing. Studies conducted in older adult patients have shown an approximate two-fold increase in risk of cardiac or cerebrovascular incidents - similar in magnitude irrespective of antipsychotic class (i.e. typical and atypical antipsychotics) - even with short term use (Gill 2007; Mittal 2011; Ray 2009; Wang 2005). Increased mortality risk was found in one meta-analysis (Schneider 2005) of 17 placebo-controlled trials of atypical antipsychotics (or second generation antipsychotics) in dementia patients. As a consequence, the US Food and Drug Administration (FDA) issued their strictest warning label or a 'black box' warning for all antipsychotic drugs due to the association with serious hazard when used in the older adult patients. A black box warning is applied to drug labelling by the FDA when there is reasonable evidence of an association of serious and, sometimes, life-threatening adverse events. Antipsychotics have also been shown to paradoxically worsen delirium severity in some patients (Agar 2016). These are important findings, as delirious patients are often frail and have multiple comorbidities (Inouye 2014). Despite the known risks and lack of strong data showing consistent benefit, physician surveys (Carnes 2003; Meagher 2010) and observational data (Briskman 2010; Hatta 2014) show exceedingly high use of antipsychotics in hospitalised delirious patients (77% to 87%).

### How the intervention might work

While relative excess of the neurotransmitter dopamine remains a leading hypothesised neurochemical substrate for delirium (Hsieh 2008; Trzepacz 1999; Trzepacz 2000; Young 1997), few

studies have examined neurotransmitter metabolism in the context of delirium trajectory (Thomas 2008; Van der Cammen 2006). The therapeutic effects of antipsychotics in delirium remain unknown, but it is postulated their effects may be mediated through a reduction of psychotic symptoms (also known as positive symptoms for patients with schizophrenia), or through sedation. There are two types of antipsychotics: first generation, also known as typical antipsychotics, (e.g. haloperidol, chlorpromazine) and second generation, also known as atypical antipsychotics, (e.g. quetiapine, olanzapine, risperidone). Both groups of antipsychotics block the brain's dopamine receptor pathways but atypical antipsychotics also act on serotonin receptors. Both are effective for managing the positive symptoms in schizophrenia (e.g. psychosis, hallucinations, agitation) but atypical antipsychotics also improve the negative symptoms such as emotional and social withdrawal. Antipsychotics are thought to help with the psychotic symptoms of delirium but have also been shown useful in individuals who have hypoactive symptoms (Boettger 2011a; Boettger 2011b; Breitbart 2002b; Ito 2007; Platt 1994). Studies investigating changes in individual delirium symptomatology in the context of antipsychotic treatment have yielded conflicting results. It appears both cognitive and noncognitive symptoms may improve to varying extents. Specifically, where some studies demonstrate a similar trajectory for both types of symptoms (Breitbart 1996; Kim 2003; Leonard 2015; Meagher 2012; Parellada 2004; Sasaki 2003), others show a more rapid recovery of noncognitive disturbances (e.g. inattention and disorientation) (Devlin 2011; Tahir 2010).

### Why it is important to do this review

Studies have shown an association between delirium and adverse outcomes such as prolonged length of hospital stay, increased hospital mortality, and higher rates of hospital readmission, institutionalisation, and functional and cognitive decline, even after adjustment for comorbidities and illness severity (Buurman 2011; Han 2010; Inouye 1998; Kakuma 2003; Leslie 2005; Levkoff 1992; McCusker 2001; McCusker 2002; Pitkala 2005; Pompei 1994; Rizzo 2001; Witlox 2010). Delirium is also known to cause distress to patients, their families, and clinical staff (Breitbart 2002a; Bruera 2009; Buss 2007; Cohen 2009; Morita 2004; Partridge 2013). The economic burden of delirium is significant: a delirious state is associated with a 20% increased risk of prolonged hospitalisation, translating to an average of more than 8 to 10 additional days in hospital (Leslie 2008; McCusker 2003; OECD 2012; WHO 2012). The annual cost of delirium has been estimated at more than USD 164 billion (Leslie 2008) in the United States, and over EUR 182 billion in 18 combined European countries (OECD 2012; WHO 2012). Delirium in hospitalised patients clearly represents a substantial public health concern. Because of its myriad iatrogenic factors (e.g. medications, immobilisation, catheterisation, and sleep impairment) (Inouye 1999), delirium is considered a preventable adverse event (Gillick 1982;

Rothschild 2000) and is used as an indicator of quality of care in the elderly (IHI 2014; Safer Healthcare Now 2005). Notwithstanding, not all cases of delirium can be prevented and the impetus to determine safe and effective treatment strategies remains important for clinicians, patients, families, and the healthcare system.

In clinical practice, antipsychotics are often the first pharmacological treatment initiated, despite conflicting evidence supporting their efficacy and reports indicating increased risk of serious adverse events, especially in the frail elderly (Gill 2007; Mittal 2011; Ray 2009; Wang 2005). Herein, we have updated the previously published Cochrane Review (Loneragan 2007). An update was warranted, given the high prevalence of hospital delirium, its associated clinical and financial burden, and the publication of new studies in the decade since the original publication.

## OBJECTIVES

Our primary objective was to assess the efficacy of antipsychotics versus nonantipsychotics or placebo on the duration of delirium in hospitalised adults (excluding critically ill populations).

Our secondary objectives were to compare the efficacy of 1) antipsychotics versus nonantipsychotics or placebo on a) delirium severity and b) delirium resolution, c) mortality, d) hospital length of stay, e) discharge disposition, f) health-related quality of life, and g) adverse effects (e.g. sudden cardiac death, QTc prolongation (i.e. increased time between the Q wave and the end of the T wave in the heart's electrical cycle), seizures, use of physical restraints); and 2) atypical versus typical antipsychotics for reducing a) delirium duration, b) delirium severity, and c) resolution, d) mortality, e) hospital length of stay, f) discharge disposition, g) health-related quality of life outcomes, and h) adverse effects (e.g. sudden cardiac death, QT prolongation, seizures, use of physical restraints).

## METHODS

### Criteria for considering studies for this review

#### Types of studies

We included all trials using a randomised or quasi-randomised design that compared an antipsychotic to a nonantipsychotic (e.g. alternative drug class such as benzodiazepines), placebo, or second antipsychotic of a different generation (secondary outcome) for the treatment of delirium. We excluded nonrandomised and cross-over interventional studies as well as observational studies.

## Types of participants

We included studies of adults (> 16 years of age) diagnosed with delirium and treated in an acute care setting. We excluded trials with a primary aim of treating delirium secondary to substance/alcohol-induced withdrawal, recruiting participants solely in out-patient, psychiatric, or long-term care settings, or in an intensive care unit (a high intensity unit). A delirium diagnosis had to have been made by a trained individual (e.g. psychiatrist, geriatrician), through formal assessment using Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria ([DSM-IV 1994](#); [DSM-IV-TR 2000](#); [DSM-V 2013](#)), or by a validated delirium screening tool (e.g. [Inouye 1990](#); [Neelon 1996](#); [Traube 2014](#)). We excluded studies where antipsychotics were evaluated for delirium prevention.

## Types of interventions

To answer our primary objective, we included studies comparing an antipsychotic to a nonantipsychotic drug (e.g. alternative drug class such as benzodiazepine) or placebo. We permitted inclusion of trials that had a nonantipsychotic group without a placebo group, as no drug has been consistently shown to be more effective than placebo. Therefore, a nonantipsychotic group was thought of as a placebo. We also included studies comparing a typical antipsychotic to an atypical antipsychotic to answer our secondary objectives. When antipsychotics are initiated to manage delirium symptoms in clinical practice, clinicians often select atypical antipsychotics over a typical antipsychotic. Therefore, we included trials that compared the two classes of antipsychotics, irrespective of inclusion of a placebo group in the study. We did not include trials that only examined two or more antipsychotics of the same class without an alternative drug or alternative antipsychotic class, or placebo.

A priori, we anticipated the selection of comparison treatments would be variable and that nonantipsychotic agents might include: alpha-2 agonists, antidepressants, benzodiazepines, cholinesterase inhibitors, melatonin or melatonin agonists, or opioids. No restrictions on dose, frequency, intensity, or duration of therapy were applied.

## Types of outcome measures

We selected outcomes pertaining to the benefits and hazards of antipsychotic drugs that are meaningful to hospitalised patients with delirium, their families, and health care professionals.

### Primary outcome

1. Total duration of delirium (days)

### Secondary outcomes

1. Delirium severity, assessed by validated instruments such as Delirium Rating Scale (e.g. DRS or DRS-98-R) ([Trzepacz 1988](#); [Trzepacz 2001](#)) and Memorial Delirium Assessment Scale (MDAS) ([Breitbart 1997](#)) (mean change from baseline to end of study period)
2. Delirium resolution (defined as reduction of DRS or DRS-98-R below a target set by the authors or complete resolution of symptoms)
3. Mortality
4. Hospital length of stay (days)
5. Hospital discharge disposition (e.g. rehabilitation, chronic care facility, home)
6. Health-related quality of life (as reported by study authors)
7. Adverse events as defined by the study authors (e.g. prolongation of the QTc interval (QT interval measures the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle), sudden cardiac death, cerebral vascular events, seizures, extrapyramidal effects, use of physical restraints, long-term cognitive impairment (e.g. change in Mini Mental Status Exam or as reported by study authors)).

## Search methods for identification of studies

### Electronic searches

Electronic search strategies were developed and tested through an iterative process by an experienced information scientist in consultation with our team. The concepts encompassed in the search strategy included: 1) population (i.e. patients in acute care settings diagnosed with delirium), 2) intervention (antipsychotics), and (3) comparators. Test searches were performed at various stages (i.e. before and after combining search terms) to ascertain the number of hits and verify capture of studies known to meet the inclusion criteria. We searched the following electronic databases from their respective dates of inception to July 20, 2017: MEDLINE (Ovid SP) (1946 to July 20, 2017); Embase (Ovid SP) (1947 to 2017 Week 28); Cochrane EBM Reviews - Central Register of Controlled Trials (CENTRAL) (July 20, 2017); CINAHL (EBSCOhost) (1982 to July 20, 2017); Thomson Reuters Web of Science (July 20, 2017) and Latin American and Caribbean Health Sciences Literature (LILACS) (1986 to July 20, 2017). We searched the Database of Abstracts of Reviews of Effects (DARE) and the Health Technology Assessment Database (HTA Database) to their second quarter of 2017 for published reviews on the review topic. Specific details regarding search strategies can be found in the appendices ([Appendix 1](#); [Appendix 2](#); [Appendix 3](#); [Appendix 4](#); [Appendix 5](#); [Appendix 6](#); [Appendix 7](#); [Appendix 8](#)). Search strategies utilised a combination of controlled vocabulary and keywords, and vocabulary and syntax were adjusted for each database. We

limited our search to randomised controlled trials, systematic reviews, and meta-analyses. We applied a filter to limit to humans, and no language restriction was imposed.

### Searching other resources

We searched conference proceedings using the Web of Science ISI Proceedings (2004 to July 2017). We searched for unpublished and ongoing trials on the following web sites: 1. [www.clinicaltrials.gov/](http://www.clinicaltrials.gov/); and 2. [www.who.int/trialsearch](http://www.who.int/trialsearch). We handsearched the reference lists of all retrieved studies for additional relevant studies. Corresponding authors of eligible trials and experts in the field were contacted to identify other potential studies. The Internet was searched using the Google search engine to find additional unpublished evidence.

### Data collection and analysis

#### Selection of studies

Each title and abstract identified from the electronic and manual searches were independently examined by two authors (LB, LR) to identify potentially eligible trials. Selected trials were screened for relevance against defined inclusion and exclusion criteria ([Appendix 9](#)). References were organised in the reference manager Endnote (Version X6, Thomson Reuters, Carlsbad, CA, USA) ([Endnotes](#)) with reasons for exclusion documented in the notes field. The studies identified as eligible were examined independently and in full to confirm inclusion. Disagreements were resolved by discussion with an independent arbiter (NS).

#### Data extraction and management

We did not blind data extractors to the identity of study authors because of our familiarity with the literature on the topic. Two authors (LB, LR) revised and piloted the previous data extraction form to ensure capture of all relevant data. Once the included trials were identified and agreed upon, four authors independently extracted data. Each study was independently examined by a pair of authors (SM and MP; JL and CB). All data extraction was confirmed by a third author (LB). Any identified duplicate reports from a single study were assembled as one reference. The 'Characteristics of included studies' table ([Characteristics of included studies](#)) was created using Review Manager ([RevMan 2014](#)). As we were interested in determining if the intervention reduced the overall severity or burden of delirium, we extracted and used the highest recorded score for delirium severity for both the intervention and control arm when multiple time points were available. For example, if DRS-98-R was scored multiple times after study enrolment, then we selected only the highest of those scores for our analyses.

### Assessment of risk of bias in included studies

Each data extractor independently assessed the risk of bias of each study, which was then verified by another author (NS). These assessments were done via a domain-based evaluation as recommended by The Cochrane Collaboration ([Higgins 2011](#)). The domains are:

1. Random sequence generation (i.e. selection bias);
2. Allocation concealment (i.e. selection bias);
3. Blinding of participants and personnel (i.e. performance bias);
4. Blinding of outcomes assessment (i.e. detection bias);
5. Incomplete outcome data (i.e. attrition bias);
6. Selective reporting; and
7. Other potential sources of bias.

For each domain, we assessed the risk of bias as 'low', 'high', or 'unclear'. Unclear risk was assigned if insufficient detail was reported, or if what happened in the study was known but the risk of bias was unclear or unknown. Once risk of bias assessment was agreed upon, each study was categorised as follows:

Low risk of bias: studies where all domains were considered 'low' risk of bias;

High risk of bias: studies where one or more domains were considered to be 'high' risk of bias; and

Unclear risk of bias: studies where one or more domains was scored as 'unclear' risk of bias.

We generated a 'risk of bias' graph figure and summary figure upon completion of assessment in Review Manager ([RevMan 2014](#)).

### Measures of treatment effect

We used risk ratios (RRs) as measures of treatment effect for dichotomous outcomes. We used between-group mean differences (MD or SMD) and standard deviations for continuous outcomes.

### Unit of analysis issues

We used data from individual participants as the unit of analysis in each trial arm. As anticipated, all included trials were parallel group design, so adjustments were not necessary for clustering.

### Dealing with missing data

When necessary, we contacted the corresponding authors to clarify issues related to data reporting and/or to obtain further study details. Missing data and dropout rates were assessed for each included study and reported in the risk of bias table. For missing data (e.g. standard deviations associated with continuous outcomes) we sent the corresponding author a maximum of three emails to request the missing information. If this failed, we used established methods to impute standard deviation values. When only medians and interquartile ranges (IQR) or ranges were reported and not available from study authors we assumed the median value to be equal to the mean to permit utilisation of all of data identified. To



estimate standard deviations we used 'IQR/1.35' or 'range/4' (for studies with  $n < 70$ ) and 'range/6' for studies with  $n > 70$ .

### Assessment of heterogeneity

Heterogeneity can be the result of an uneven distribution of important clinical and methodological effect modifiers across studies or across comparisons. We assessed each trial for statistical and clinical heterogeneity. We evaluated statistical heterogeneity using the  $I^2$  statistic and the  $X^2$  test of homogeneity with  $p < 0.05$  indicative of heterogeneity. We applied the categorisation values described by Higgins: low (0% to 40%), moderate (30% to 60%), substantial (50% to 90%), and considerable (75% to 100%) heterogeneity (Higgins 2003). We qualitatively assessed clinical heterogeneity by examining delirium management strategies in each trial (e.g. treatment dose, use of rescue medications or chemical restraint when primary treatment fails, non-drug treatment strategies such as noise reduction or improving the day-night cycle, medications avoided, physical restraint) as well as country of study origin, year of study publication, and single centre versus multicentre study.

### Assessment of reporting biases

We planned construction and visual inspection of funnel plots to assess for possible publication bias in Review Manager 5 (RevMan 2014) for analyses where  $> 10$  studies were available. We planned to test for funnel plot asymmetry using the test proposed by Egger (Egger 1997), but there were insufficient studies to proceed with this step.

### Data synthesis

Two authors (LB, BH) entered data in Revman 5 (RevMan 2014). Three authors (LB, BH, DF) conducted the analyses and reported summary statistics for the data. We synthesised dichotomous data with risk ratios (RR) and 95% confidence intervals (CI) using the Mantel-Haenszel random-effects model (REM) to allow for adjustments that incorporated variation both within and between studies (DeMets 1987). Continuous outcomes (e.g. duration of delirium, hospital length of stay) were synthesised as pooled mean differences (MD), or standardised mean differences (SMD) (where measurement scales varied across studies) with 95% CIs using random-effects inverse variance methods. For continuous end points that involved an analysis of changes from baseline in each group, where necessary, a correlation coefficient was used to estimate the standard deviation associated with mean change in each group. We considered  $P < 0.05$  (two sided) as significant.

### Subgroup analysis and investigation of heterogeneity

We planned the following subgroup analyses to determine if the efficacy and safety of antipsychotics were influenced by: 1) age ( $< 65$  versus  $\geq 65$  years); and 2) history of dementia.

### Sensitivity analysis

We conducted sensitivity analyses to explore the effect on the pooled estimate of including only studies at low risk of bias in all but one domain and those that included a placebo group.

### Data presentation - 'Summary of findings' table

We used the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) (Guyatt 2008) approach to assess the quality of the supporting evidence associated with selected outcomes. The findings are presented using a 'Summary of findings' (SoF) table summarising the amount of data identified, within-study risk of bias, directness of evidence, data heterogeneity, and precision of effect estimates. The SoF table was generated using GRADEpro software (GRADEpro GDT 2015). We selected the following outcomes a priori as being relevant for clinical practice: duration of delirium, severity of delirium, delirium resolution, mortality, hospital length of stay, and incidence of adverse effects.

## RESULTS

### Description of studies

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#); [Characteristics of studies awaiting classification](#); [Characteristics of ongoing studies](#)

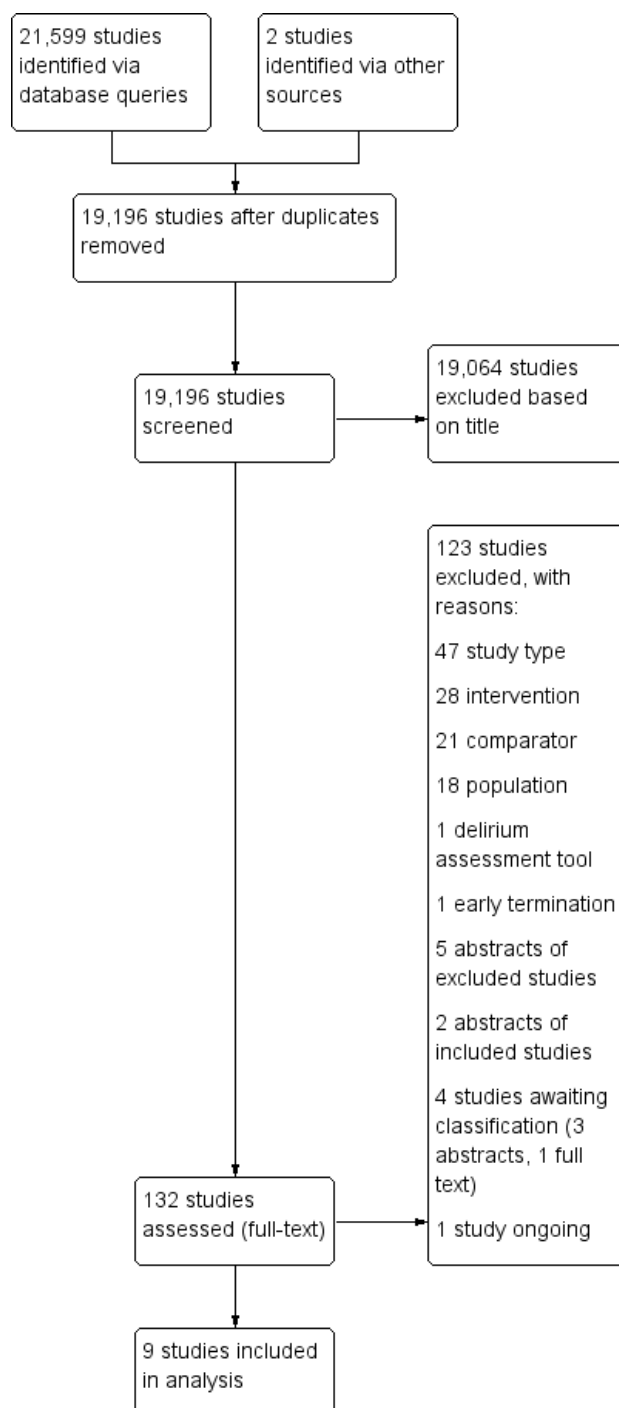
We included randomised and quasi-randomised controlled trials of adult hospitalised non-ICU patients treated for delirium. We identified eligible trials with an intervention arm including an antipsychotic drug. Delirium management for control arms included a nonantipsychotic drug (e.g. alternative drug class such as benzodiazepines), placebo, or secondary antipsychotic of alternative class (i.e. typical versus atypical).

### Results of the search

We reported the results of the search outlined above in [Figure 1](#). The initial electronic database query yielded 21,599 citations. We retrieved 132 references for full-text assessment. We identified nine studies meeting inclusion criteria, and excluded the remaining 123. We classified four studies as awaiting classification ([Characteristics of studies awaiting classification](#)): one full publication (Nakamura 1997) and three conference abstracts (Djokic 2008; Jung Jin 2009; Lee 2013). We identified two trial registrations for further consideration. We classified one study as meeting inclusion criteria and ongoing (NCT02345902; [Characteristics of ongoing studies](#)), and the other as a duplicate of a study published in full and already included in the review (Hu 2004; [Characteristics of included studies](#)). When this latter study was translated into the English language, the primary author's first and last names were

reversed. We identified this upon closer inspection and classified the second trial registration as a duplicate.

**Figure 1. PRISMA flow diagram of search results.**



## Included studies

See: [Characteristics of included studies](#) table.

We included nine randomised trials with a total of 727 participants ([Agar 2016](#); [Breitbart 1996](#); [Grover 2011](#); [Grover 2016](#); [Han 2004](#); [Hu 2004](#); [Lin 2008](#); [Maneeton 2013](#); [Tahir 2010](#)). We provide detailed descriptions of each study in the [Characteristics of included studies](#) table. Sample sizes of trials ranged from 24 ([Han 2004](#)) to 247 ([Agar 2016](#)) participants. Four of the identified trials included more than two study arms ([Agar 2016](#); [Breitbart 1996](#); [Grover 2011](#); [Hu 2004](#)). Only a single study ([Agar 2016](#)) included multiple sites; all others had a single centre design. The trials were conducted in a number of countries: Australia ([Agar 2016](#)); China ([Hu 2004](#)); India ([Grover 2011](#); [Grover 2016](#)); Korea ([Han 2004](#)); Taiwan ([Lin 2008](#)); Thailand ([Maneeton 2013](#)); United States ([Breitbart 1996](#)); and United Kingdom ([Tahir 2010](#)). All studies included hospitalised patient populations: medical only ([Breitbart 1996](#); [Hu 2004](#); [Maneeton 2013](#)), mixed medical and surgical ([Grover 2011](#); [Grover 2016](#); [Han 2004](#); [Tahir 2010](#)), and palliative ([Agar 2016](#); [Lin 2008](#)). One trial specifically evaluated participants with dementia ([Hu 2004](#)). The mean reported age of participants across trials ranged from 44 ([Grover 2011](#)) to 84 ([Tahir 2010](#)) years; 22% ([Grover 2016](#)) to 71% ([Tahir 2010](#)) of participants were female. Six studies ([Agar 2016](#); [Breitbart 1996](#); [Grover 2011](#); [Han 2004](#); [Maneeton 2013](#); [Tahir 2010](#)) provided details of funding sources; one trial received pharmaceutical industry funding ([Tahir 2010](#)).

Four trials compared one or more antipsychotic drug to a nonantipsychotic or placebo ([Agar 2016](#); [Breitbart 1996](#); [Hu 2004](#); [Tahir 2010](#)), three of these trials included a placebo group ([Agar 2016](#); [Hu 2004](#); [Tahir 2010](#)), and one compared antipsychotics (haloperidol or chlorpromazine) to the benzodiazepine lorazepam ([Breitbart 1996](#)). Seven trials compared a typical to an atypical antipsychotic drug ([Agar 2016](#); [Grover 2011](#); [Grover 2016](#); [Han 2004](#); [Hu 2004](#); [Lin 2008](#); [Maneeton 2013](#)). Of these, two ([Agar 2016](#); [Hu 2004](#)) also included a placebo group (i.e. 3-arm studies). Haloperidol was the most commonly studied antipsychotic, evaluated in all but one trial ([Tahir 2010](#)). All trials titrated study drug based on symptom response. The duration of therapy was variable and included three- ([Agar 2016](#)), six- ([Breitbart 1996](#); [Grover 2011](#); [Grover 2016](#)), seven- ([Han 2004](#); [Hu 2004](#); [Lin 2008](#); [Maneeton 2013](#)), and ten-day ([Tahir 2010](#)) administration. The use of rescue drugs such as benzodiazepines for breakthrough agitation was permitted in five trials ([Agar 2016](#); [Grover 2011](#);

[Grover 2016](#); [Lin 2008](#); [Tahir 2010](#)), prohibited in three ([Hu 2004](#); [Maneeton 2013](#); [Breitbart 1996](#)), and not reported in one ([Han 2004](#)). No trial reported on the use of physical restraints or sitters/personal attendants.

All trials used some combination of DSM criteria ([DSM-IV 1994](#); [DSM-IV-TR 2000](#); [DSM-V 2013](#)) or the Confusion Assessment Method (CAM) ([Inouye 1990](#)), or both, to detect delirium for study enrolment; subjects in all included studies were screened daily. Cointerventions for delirium management such as reorientation, family support, and environmental manipulations were used in five studies ([Agar 2016](#); [Grover 2011](#); [Grover 2016](#); [Hu 2004](#); [Maneeton 2013](#)) and not reported in the remaining four ([Breitbart 1996](#); [Han 2004](#); [Lin 2008](#); [Tahir 2010](#)).

## Excluded studies

See: [Characteristics of excluded studies](#) table.

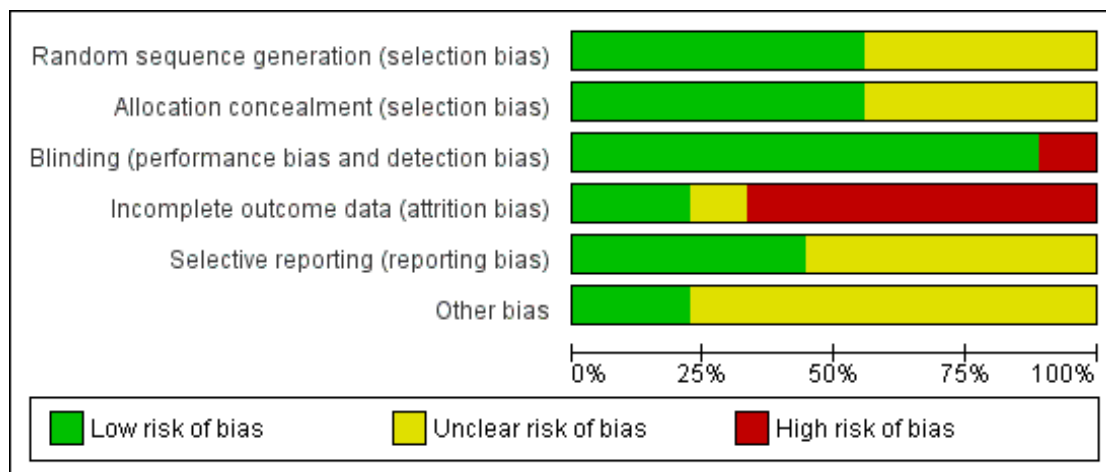
We excluded ten randomised trials because the population of interest was limited to critically ill individuals ([Al Qadheeb 2016](#); [Atalan 2013](#); [Bakri 2015](#); [Devlin 2010](#); [Girard 2010](#); [Hakim 2012](#); [Page 2013](#); [Reade 2009](#); [Reade 2016](#); [Skrobik 2014](#)). These trials are included in the Cochrane protocol ACE311 'Pharmacological interventions for the treatment of delirium in critically ill patients' ([Burry 2015](#)) using the operational definition of critical care/intensive care applied by this Cochrane division. We excluded five additional studies ([Jung 2009](#); [Jung 2010](#); [Kim 2010](#); [Lee 2005](#); [Sakong 2010](#)) because of lack of adequate comparator group. These five studies evaluated the effect of antipsychotic(s) on hospitalised, non-critically ill participants with delirium but did not include a nonantipsychotic arm or they compared two antipsychotics of the same class (e.g. atypical versus atypical) without a third group that included a placebo or nonantipsychotic drug.

## Risk of bias in included studies

The 'Risk of bias' tables present details on the performance of the included trials for each risk of bias domain. A summary of our judgement of the methodological quality of the included studies is depicted in [Figure 2](#) and [Figure 3](#). Only one study ([Agar 2016](#)) was scored as low risk of bias across all domains. The remaining studies scored unclear risk of bias in one or more domains, or had a combination of unclear and high risk of bias across multiple domains. In particular, [Hu 2004](#) scored high risk of bias across two domains..



**Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.**



**Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.**

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Agar 2016						
Breitbart 1996						
Grover 2011						
Grover 2016						
Han 2004						
Hu 2004						
Lin 2008						
Maneeton 2013						
Tahir 2010						

### Allocation (selection bias):

Five studies (Agar 2016; Breitbart 1996; Grover 2016; Maneeton 2013; Tahir 2010) specified the use of randomisation tables. The method of sequence generation was not reported in the manuscript or available from the authors for the remaining four trials (Grover 2011; Han 2004; Hu 2004; Lin 2008), therefore, we scored these as unclear risk of bias.

We judged five studies (Agar 2016; Breitbart 1996; Grover 2011; Maneeton 2013; Tahir 2010) to have low risk of selection bias based on their allocation concealment measures. Two studies (Agar 2016; Tahir 2010) used sealed opaque envelopes and another used a pharmacist (Breitbart 1996) not otherwise involved in patient care to dispense the study drug. In Grover 2011, the randomisation and study drug dose adjustments were carried out by one investigator who did not assess outcomes. In Maneeton 2013, identical capsules were used to dispense the study drug. We judged the remaining studies (Grover 2016; Han 2004; Hu 2004; Lin 2008) to have unclear risk of selection bias due to insufficient or no detail to assess allocation concealment.

### Blinding (performance bias and detection bias):

We judged all studies but one (Hu 2004) to have low risk of blinding bias. Four studies (Agar 2016; Breitbart 1996; Maneeton 2013; Tahir 2010) were double-blinded. A single-blind design was used in three studies (Grover 2011; Grover 2016; Lin 2008) that specifically reported the delirium assessment was performed by a standard blinded assessor. Although Han 2004 study was stated as double-blind, this was unlikely as the study drugs were not stated to be identical. However, one psychiatrist, blind to treatment group, performed the delirium assessments. We judged Hu 2004 study to have high risk of bias as it was not possible to blind subcutaneous haloperidol and enteral olanzapine, unless a double-dummy design was used. As no details were provided, we assumed the drug formulation was unblinded.

### Incomplete outcome data (attrition bias):

We judged three studies (Agar 2016; Maneeton 2013; Tahir 2010) to have low risk of attrition bias because all used intention-to-treat analysis or had no missing data. We judged one study (Breitbart 1996) to have unclear risk of attrition bias. The lorazepam arm in Breitbart 1996 was discontinued early due to adverse events, but available data were used in the analysis. We judged five studies (Grover 2011; Grover 2016; Han 2004; Hu 2004; Lin 2008) to have high risk of attrition bias due to incomplete data or missing participants. In Grover 2011, ten participants did not complete the study; six could not be assessed at least once due to worsening clinical status, and four left hospital against medical advice.

In Grover 2016, seven participants did not complete the study; four could not be assessed because they left against medical advice, one quetiapine participant received injectable haloperidol for symptom management, and two could not be started on the study drug because of worsening clinical status. In the Han 2004 study, four participants did not complete the study, three due to medical complications and one due to spousal refusal; these participants were not included in the analysis. The Hu 2004 study made no mention of how attrition was factored into the statistical analysis despite reporting five participants not completing the study (one death, one leaving due to financial reasons, one discharge, and two withdrawals). Lastly, Lin 2008 did not report the total number of participants enrolled or lost to follow-up.

### Selective reporting (reporting bias):

We found four trials were registered (Agar 2016; Hu 2004; Maneeton 2013; Tahir 2010) and, therefore, it was possible to examine reporting bias. These trials were deemed at low risk of bias. For the remaining studies, we scored them as at unclear risk of bias.

### Other potential sources of bias:

Referral bias was a potential issue for four trials (Grover 2011; Grover 2016; Lin 2008; Maneeton 2013) where participants were recruited specifically from referrals to psychiatry services. Sample size calculations were not provided for five trials (Breitbart 1996; Grover 2011; Grover 2016; Han 2004; Lin 2008) so it was unclear if adequate power was attained. Two trials (Maneeton 2013; Tahir 2010) did not meet the required sample size. In one study (Maneeton 2013), 34 participants per group were needed to have adequate power to detect a meaningful difference in DRS-R-98 score; however, the final numbers were 24 and 28 participants in the quetiapine and haloperidol groups, respectively. The sample size calculation was reported in the second study (Tahir 2010), however the trial was stopped early at the request of the manufacturer due to the FDA's concern on the use of antipsychotic medication in the elderly. The study was therefore underpowered. Finally, one included study (Tahir 2010) permitted lorazepam injection for rescue, but all participants who received it were in the quetiapine group. It was unclear how lorazepam administration in only one group would influence results.

### Effects of interventions

See: [Summary of findings for the main comparison Antipsychotics versus nonantipsychotics or placebo for the treatment of delirium in hospitalised patients](#); [Summary of](#)

## findings 2 Typical versus atypical antipsychotics for treatment of delirium in hospitalised patients

See: [Summary of findings for the main comparison](#); [Summary of findings 2](#)

We present below our analyses for our primary outcome, duration of delirium, and our secondary outcomes of severity of delirium, delirium resolution, mortality, hospital length of stay and discharge disposition, health-related quality of life, and adverse events. For each outcome, we present first the results for the comparison of an antipsychotic versus nonantipsychotic or placebo and then the class comparison of typical versus atypical antipsychotic.

### Duration of delirium

#### Antipsychotic versus nonantipsychotic drug or placebo

Duration of delirium was not reported for any of the four trials comparing an antipsychotic to a nonantipsychotic drug.

#### Typical versus atypical antipsychotic drug

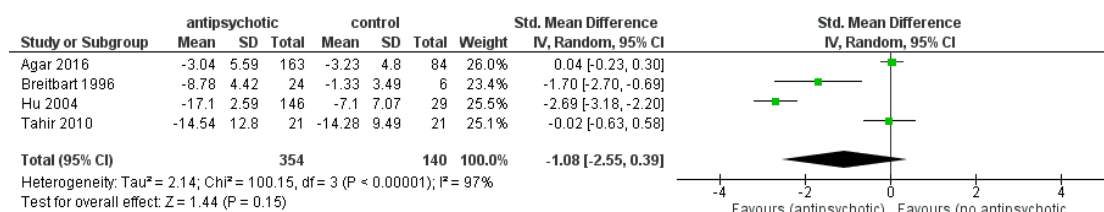
Duration of delirium was not reported for any trial comparing typical versus atypical antipsychotics drugs.

### Delirium severity

#### Antipsychotic versus nonantipsychotic drug or placebo

Delirium severity was reported for four studies ([Agar 2016](#); [Breitbart 1996](#); [Hu 2004](#); [Tahir 2010](#)). Delirium severity was scored with different tools: the DRS ([Breitbart 1996](#); [Hu 2004](#)), DRS-98-R ([Tahir 2010](#)), and MDAS ([Agar 2016](#)), assessed at baseline and at the end of the study. Three of the studies were double-blind so delirium assessments were blinded. The pooled result indicated no difference in delirium severity (SMD -1.08, 95% CI -2.55 to 0.39; four studies; 494 participants; [Analysis 1.1](#); [Figure 4](#)). There was substantial heterogeneity ( $I^2 = 97\%$ ). We assessed this as very low-quality evidence (downgraded due to risk of bias, inconsistency and imprecision). For sensitivity analyses, we repeated the analysis by i) removing trial(s) that did not have a placebo group ([Breitbart 1996](#)) (SMD -0.89, 95% CI -2.64 to 0.86; three studies; 464 participants;  $I^2 = 98\%$ ; [Analysis 1.2](#)) and ii) including only trials with low risk of bias (SMD 0.03, 95% CI -0.22 to 0.27; 289 participants;  $I^2 = 0\%$ ; [Analysis 1.3](#)).

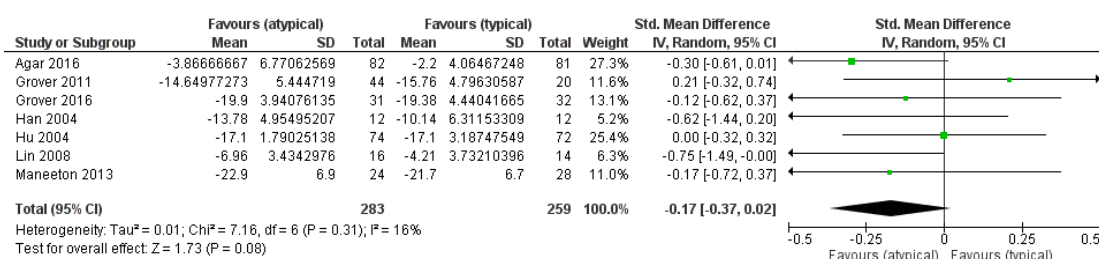
**Figure 4. Forest plot of comparison: 2 severity of delirium, outcome: 2.1 antipsychotic versus no antipsychotic.**



### Typical versus atypical antipsychotic drug

Seven studies (Agar 2016; Grover 2011; Grover 2016; Han 2004; Hu 2004; Lin 2008; Maneeton 2013) reported this outcome. All but one trial (Han 2004) had delirium assessment by a psychiatrist or nurse blinded to the status of treatment. Delirium severity was scored with the DRS (Han 2004; Hu 2004; Lin 2008), DRS-98-R (Grover 2011; Grover 2016; Maneeton 2013) and MDAS (Agar 2016), assessed at baseline and at the end of study treatment. The pooled result showed no difference in delirium severity (SMD -0.17, 95% CI -0.37 to 0.02; 542 participants, Analysis 1.4; Figure 5). There was a low degree of heterogeneity ( $I^2 = 16\%$ ). We assessed this as low-quality evidence (downgraded due to risk of bias, inconsistency). It was not feasible to conduct the sensitivity analysis including only trials at low risk of bias.

**Figure 5. Forest plot of comparison: 1 severity of delirium, outcome: 1.4 atypical antipsychotic versus typical antipsychotic.**



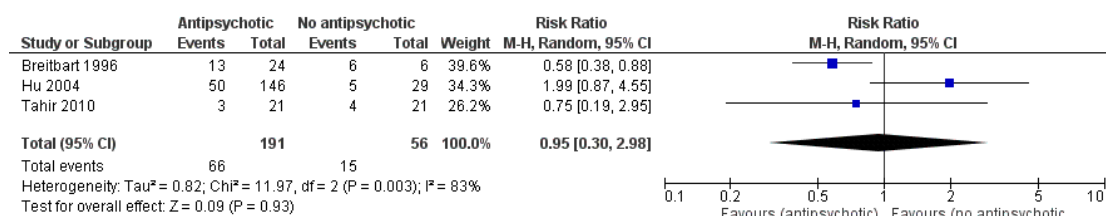
### Delirium resolution

#### Antipsychotic versus nonantipsychotic drug or placebo

Delirium resolution was reported for three studies (Breitbart 1996; Hu 2004; Tahir 2010). The definition of resolution applied in the trials varied: complete alleviation of symptoms (Hu 2004), alleviation of symptoms to below an unspecified diagnostic threshold (Breitbart 1996), and a cutoff of DRS-R98 < 15 on day 7 (Tahir 2010). Two of the studies were double-blind so delirium assess-

ments were blinded. The pooled result indicated no significant difference in overall delirium resolution (RR 0.95, 95% CI 0.30 to 2.98; three studies, 247 participants; Analysis 2.1; Figure 6). There was a high degree of heterogeneity ( $I^2 = 83\%$ ). We assessed this as very low-quality evidence (downgraded due to risk of bias, inconsistency, imprecision). As a sensitivity analysis, we (Analysis 2.2) included only trials with a placebo group (Hu 2004; Tahir 2010). The pooled result indicated no significant difference in overall delirium resolution (RR 1.43, 95% CI 0.58 to 3.54; two studies; 217 participants) but with less heterogeneity ( $I^2 = 30\%$ ). It was not feasible to conduct the sensitivity analysis including only trials at low risk of bias.

**Figure 6. Forest plot of comparison: 3 resolution, outcome: 3.1 antipsychotic versus no antipsychotic.**

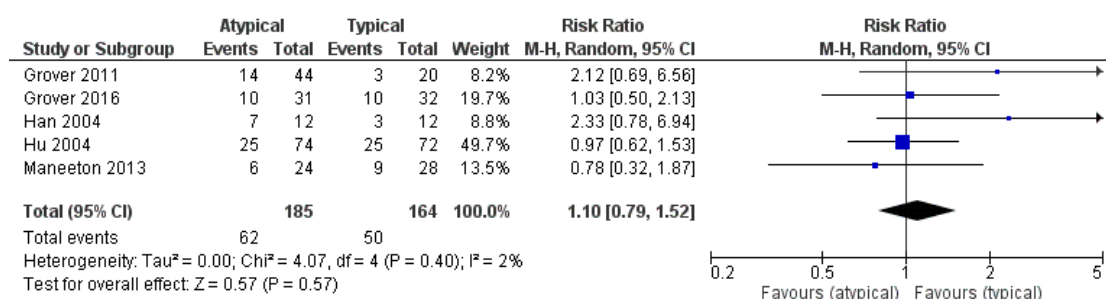


### Typical versus atypical antipsychotic drug

Delirium resolution was reported for five studies (Grover 2011; Grover 2016; Han 2004; Hu 2004; Maneeton 2013). The definition of resolution varied in the trials: DRS-R98 < 10 (Grover 2011; Grover 2016), DRS-R98 < 12 (Maneeton 2013), MDAS < 13 (Han 2004), and complete alleviation of symptoms (Hu 2004). Four of the trials (Grover 2011; Grover 2016; Han 2004;

Maneeton 2013) were blinded studies and had blinded delirium assessments. The pooled result indicated no significant difference in overall delirium resolution (RR 1.10, 95% CI 0.79 to 1.52; 349 participants; Analysis 2.3; Figure 7). There was a low degree of heterogeneity ( $I^2 = 2\%$ ). We assessed this as low-quality evidence (downgraded due to risk of bias, inconsistency). It was not feasible to conduct the sensitivity analysis including only trials at low risk of bias.

**Figure 7. Forest plot of comparison: 2 resolution, outcome: 2.3 atypical antipsychotic versus typical antipsychotic.**



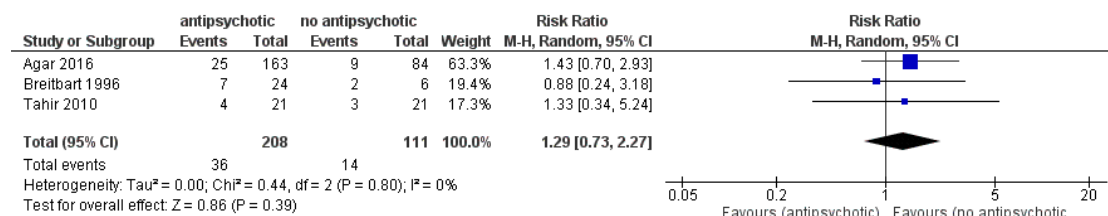
### Mortality

#### Antipsychotic versus nonantipsychotic drug or placebo

Mortality was reported for three studies (Agar 2016; Breitbart 1996; Tahir 2010). The end point was measured at study day three (Agar 2016), within one week of study completion (Breitbart

1996), and at day 30 (Tahir 2010). The pooled result indicated no statistical difference in mortality (RR 1.29, 95% CI 0.73 to 2.27; three studies, 319 participants; Analysis 3.1; Figure 8). There was a low degree of heterogeneity ( $I^2 = 0\%$ ). We assessed this as low-quality evidence (downgraded due to risk of bias, imprecision). We conducted a sensitivity analysis with only trials that included a placebo group (Analysis 3.2). The pooled result indicated no statistical difference in mortality (RR 1.41, 95% CI 0.75 to 2.66; two studies, 289 participants;  $I^2 = 0\%$ ).

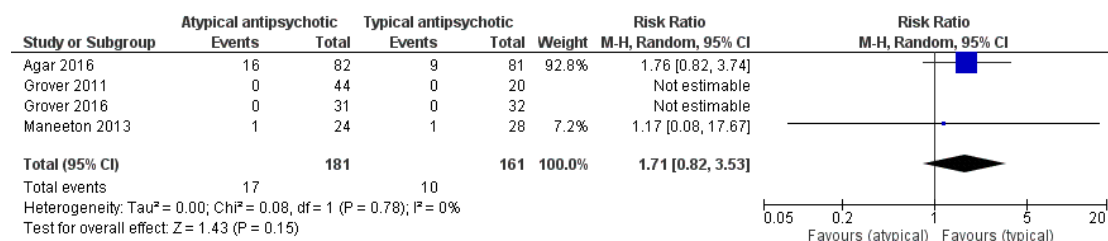
**Figure 8. Forest plot of comparison: 3 mortality, outcome: 3.1 antipsychotic versus no antipsychotic.**



### Typical versus atypical antipsychotic drug

Mortality was reported for four studies (Agar 2016; Grover 2011; Grover 2016; Maneeton 2013). Time to end point was measured at study day three (Agar 2016) and within one week of study enrolment (Grover 2011; Grover 2016; Maneeton 2013). Mortality was very low and no deaths were reported in two studies (Grover 2011; Grover 2016). The pooled result indicated no statistical difference in overall mortality (RR 1.71, 95% CI 0.82 to 3.35; four studies; 342 participants; Analysis 3.3; Figure 9). There was a low degree of heterogeneity ( $I^2 = 0\%$ ). We assessed this as low-quality evidence (downgraded due to risk of bias, imprecision).

**Figure 9. Forest plot of comparison: 3 mortality, outcome: 3.3 atypical antipsychotic versus typical antipsychotic.**



### Hospital length of stay (days)

#### Antipsychotic versus nonantipsychotic drug or placebo

No trials reported hospital length of stay, and attempts to obtain data from corresponding study authors proved unsuccessful.

#### Typical versus atypical antipsychotic drug

No trials reported hospital length of stay, and attempts to obtain data from corresponding study authors proved unsuccessful.

#### Hospital discharge disposition

#### Antipsychotic versus nonantipsychotic drug or placebo

No trials reported hospital discharge disposition, and attempts to obtain data from corresponding study authors proved unsuccessful.

### Typical versus atypical antipsychotic drug

No trials reported hospital discharge disposition, and attempts to obtain data from corresponding study authors proved unsuccessful.

### Health-related quality of life

#### Antipsychotic versus nonantipsychotic drug or placebo

No trials reported health-related quality of life, and attempts to obtain data from corresponding study authors proved unsuccessful.

### Typical versus atypical antipsychotic drug

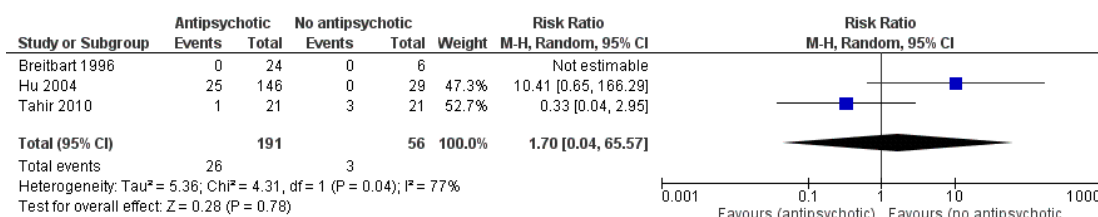
No trials reported health-related quality of life and attempts to obtain data from corresponding study authors proved unsuccessful.

### Adverse events

#### Antipsychotic versus nonantipsychotic drug or placebo

No trials reported the use of physical restraints, long-term cognitive measures, or incidence of seizures, cerebrovascular events, sudden cardiac death or QTc abnormalities. Extrapyramidal symptoms (EPS) were reported for three studies (Breitbart 1996; Hu 2004; Tahir 2010). EPS was assessed using the Extrapyramidal Symptom Rating Scale in two trials (Breitbart 1996; Hu 2004), and the method was not reported in the other trial (Tahir 2010). The overall number of reported EPS events was low in the trials. The pooled result indicated the risk of EPS with antipsychotics was not statistically increased (RR 1.70, 95% CI 0.04 to 65.57; 247 participants; Analysis 4.1; Figure 10). There was substantial heterogeneity ( $I^2 = 77\%$ ). We assessed the evidence as very low-quality evidence (downgraded due to risk of bias, inconsistency, imprecision). One additional study (Agar 2016) reported significantly greater mean extrapyramidal effects in risperidone versus placebo-treated participants using mixed effects modelling, without specifying the actual summary measure used (0.73, 95% CI 0.09 to 1.37,  $P = 0.03$ ) and haloperidol versus placebo-treated (0.79, 95% CI 0.17 to 1.41,  $P = 0.01$ ) participants on each study day. Raw data were not available, thus, we were unable to pool these data with the other trials.

**Figure 10. Forest plot of comparison: 4 adverse event, outcome: 4.1 antipsychotic versus no antipsychotic (EPS).**



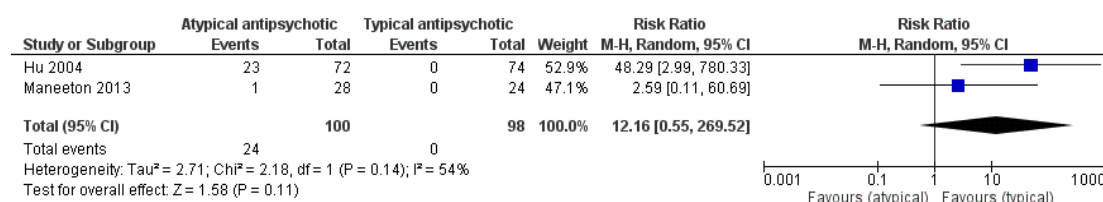
### Typical versus atypical antipsychotic drug

No trials reported the use of physical restraints, long-term cognitive measures, cerebrovascular events, sudden cardiac death or QTc abnormalities. One trial (Maneeton 2013) reported on seizures with one seizure in the quetiapine group and no seizures in the haloperidol group. This trial also reported arrhythmias with one AV block episode in the haloperidol group and no events in the quetiapine group. Two trials (Hu 2004; Maneeton 2013) reported EPS symptoms. EPS was assessed using the Extrapyramidal Sym-

tom Rating Scale in one trial (Hu 2004) and the other with MSAS (Maneeton 2013). The overall number of participants experiencing any EPS symptoms was low. The pooled results showed no statistical increased risk of EPS with typical antipsychotics compared to atypical antipsychotics (RR 12.16, 95% CI 0.55 to 269.52; two studies; 198 participants; Analysis 4.2; Figure 11). There was a moderate degree of heterogeneity ( $I^2 = 54\%$ ). We assessed the evidence as very low-quality evidence (downgraded due to risk of bias, inconsistency, imprecision).



**Figure 11. Forest plot of comparison: 4 adverse event, outcome: 4.2 atypical antipsychotic versus typical antipsychotic (EPS).**



### Subgroup analysis and investigation of heterogeneity

We intended to conduct subgroup analyses exploring the effects of controlling for age and history of dementia. However, due to the small number of included studies and lack of relevant data, these analyses could not be conducted. We found substantial heterogeneity in analysis 1.1 ([Analysis 1.1](#)), 1.2 ([Analysis 1.2](#)) and 4.1 ([Analysis 4.1](#)). When we removed the studies not at low risk of bias ([Breitbart 1996](#) and [Hu 2004](#); [Analysis 1.3](#)) there is no longer such variability. We believe the use of different tools to measure the outcome may potentially explain the variation identified.

## ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Typical versusAtypical antipsychotics for treatment of delirium in hospitalised patients						
<b>Patient or population:</b> delirious patients <b>Settings:</b> hospital wards, not ICU <b>Intervention:</b> typical antipsychotic drug <b>Comparison:</b> atypical antipsychotic drug						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Atypical antipsychotic drug	Typical antipsychotic drug				
<b>Duration of delirium</b> Follow-up: days						This outcome was not reported in any trial.
<b>Delirium resolution</b> DRS, DRS-R98 <sup>1</sup> Follow-up: 7 days	<b>Study population</b>		<b>RR 1.1</b> (0.79 to 1.52)	349 (5 studies)	⊕⊕○○ <b>Low-quality:</b> we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different. <sup>2,3</sup>	
	<b>305 per 1000</b>	<b>335 per 1000</b> (241 to 463)				
	<b>Moderate</b>					
	<b>313 per 1000</b>	<b>344 per 1000</b> (247 to 476)				
<b>Delirium severity</b> DRS, DRS-R98 <sup>1</sup> Follow-up: 7 days	The mean DRS-R98 score was 29.7 (SD 4.6) at the end of study. <sup>10</sup>	The standardised delirium severity score was <b>0.17 points lower</b> in the intervention group (0.37 lower to 0.02 higher)		542 (7 studies)	⊕⊕○○ <b>Low-quality:</b> we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a	SMD -0.17 (-0.37 to 0.02)

				possibility that it is substantially different. <sup>4,5</sup>	
<b>Mortality</b> Follow-up: 7 days	<b>Study population</b>		<b>RR 1.71</b> (0.82 to 3.53)	342 (4 studies)	⊕⊕○○ <b>Low-quality:</b> we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different. <sup>6</sup>
	<b>62 per 1000</b>	<b>106 per 1000</b> (51 to 219)			
	<b>Moderate</b>				
	<b>18 per 1000</b>	<b>31 per 1000</b> (15 to 64)			
<b>Hospital length of stay</b> Follow-up: days					This outcome was not reported in any trial.
<b>Adverse Effects - EPS</b> Follow-up: 7 days	<b>Study population</b>		<b>RR 12.16</b> (0.55 to 269.52)	198 (2 studies)	⊕○○○ <b>Very low-quality:</b> we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect. <sup>7,8,9</sup>
	<b>0 per 1000</b>	<b>0 per 1000</b> (0 to 0)			
	<b>Moderate</b>				
	<b>0 per 1000</b>	<b>0 per 1000</b> (0 to 0)			

\*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**CI:** Confidence interval; **DRS:** Delirium Rating Scale; **DRS-R98** = Delirium Rating Scale Revised 98; **EPS:** Extrapyramidal Symptoms; **RR:** Risk ratio

GRADE Working Group grades of evidence

**High quality:** Further research is very unlikely to change our confidence in the estimate of effect.

**Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

**Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low quality:** We are very uncertain about the estimate.

<sup>1</sup> DRS = Delirium Rating Scale; DRS-R98 = Delirium Rating Scale Revised 98

<sup>2</sup> All included trials had risk of bias.

- <sup>3</sup> Delirium resolution was measured with different tools at variable time points using different thresholds.
- <sup>4</sup> Only 1 of 7 trials was considered low risk of bias across all domains. Six of the seven trials had blinded delirium assessment.
- <sup>5</sup> Delirium severity was measured with different tools at variable time points.
- <sup>6</sup> Low number of events.
- <sup>7</sup> All trials at risk of bias.
- <sup>8</sup> Variable tools used to assess.
- <sup>9</sup> Few events and wide confidence intervals.
- <sup>10</sup> Assumed risk taken from [Maneeton 2013](#).

## DISCUSSION

### Summary of main results

We identified nine randomised trials evaluating antipsychotics for treatment of delirium in hospitalised, non-ICU patients. Four of the trials compared antipsychotics to nonantipsychotic drugs or placebo and seven compared typical to atypical antipsychotics. We found no evidence for determining the effect of antipsychotic drugs (as a class or by type) on duration of delirium. The current evidence does not support the use of an antipsychotic drug to reduce delirium severity, shorten time to resolution, or reduce mortality. We found no evidence to determine the effect of antipsychotics on length of hospital stay or health-related quality of life. Low-quality evidence showed adverse drug events were infrequently assessed but available data indicated extrapyramidal side effects were not more common with antipsychotic drugs compared to nonantipsychotic drugs or placebo and typical antipsychotics (e.g. haloperidol) were comparable to atypical antipsychotics (e.g. risperidone).

### Overall completeness and applicability of evidence

The original version of this Cochrane Review included three trials (Loneragan 2007). We had anticipated finding a large number of new trials investigating antipsychotics for a number of reasons, including the known association between delirium and adverse patient outcomes, that delirium is deemed publicly important and is an indicator of quality of care in the elderly, and the fact that the 2010 NICE guidelines recommended further research. Despite the ten-year time lapse since the original version of this review, the body of evidence for treatment of delirium for hospitalised non-ICU patients with antipsychotic drugs remains limited and fraught with issues. Although we identified nine trials for inclusion, none of the trials reported on delirium duration, length of hospital stay, hospital discharge destination, health-related quality of life, and many of the adverse events we perceived were important to patients, families and clinicians. Most of the studies were single centre studies with insufficient sample size, heterogeneous study populations, and at risk of bias. Only one trial was an adequately powered trial that included a placebo group (Agar 2016) with low risk of bias across all domains. It is also important to note there were differences in how some of the outcomes were measured in the trials. For example, there were sufficient studies to pool for the outcomes, delirium severity and resolution of symptoms, but different tools were used and the time points assessed were not consistent. Our planned subgroup analyses to determine if there were differences in effect/safety in the older or dementia participant populations could not be addressed because of lack of data. We had anticipated finding more evidence in these populations as delirium is common in these subgroups.

### Quality of the evidence

We scored the risk of bias for each trial and used GRADEpro software to inform the generation of evidence quality statements. Of the nine randomised controlled trials included in this review, only one trial scored low risk of bias across all domains. Although this review included only randomised controlled trials, the quality of evidence was downgraded for risk of bias, inconsistency, or imprecision. There were some notable design issues of these trials that should be factored into future trials. Guidelines suggest antipsychotics only be considered once non-drug strategies are considered ineffective or insufficient for the distressed patient. Only half of the identified trials reported that non-drug strategies were used during the study period and details of the interventions applied were not provided. Also, the use of rescue therapies for agitation, such as benzodiazepines, was not consistently reported. Physical restraint use was not reported in any trial. Use of chemical and physical restraint as rescue therapy presents an opportunity to introduce bias and thus should be standardised and reported in future trials. There was heterogeneity for some outcomes and their measurement methods. For the outcomes, severity and resolution of delirium, variable tools were used, different definitions or thresholds were applied, and the outcomes were assessed at different time points. In future trials, one must also consider the fact that delirium severity rating scales tend to focus more on hyperactive delirium, which is less common, rather than hypoactive delirium.

### Potential biases in the review process

This review followed the Cochrane procedures and there were only a small number of amendments to the review process (outlined in [Differences between protocol and review](#)).

### Agreement and disagreements with other studies or reviews

The original version of this Cochrane Review did not answer the specific question of the effect of antipsychotics compared to no antipsychotics on delirium outcomes in hospitalised non-ICU patients. We believe it is critical to first understand if antipsychotics as a class are effective and safe for management of delirium before comparing typical and atypical antipsychotics. We have expanded on the original review to answer this specific question before comparing typical and atypical antipsychotics. On the advice of Cochrane, we also narrowed the population by excluding the clinically unique critically ill patient population.

Our principal finding was consistent with a recent comprehensive review by Neufeld and colleagues (Neufeld 2016). Neufeld and colleagues did not find the available evidence supported antipsychotic use for prevention or treatment of delirium in any hospitalised patient population. This review included studies of any

design (prospective or historical cohort, case-control, and other observational designs) and they included both ICU and non-ICU participant populations. The generated outcomes were based on nearly all trials enrolling only critically ill participants. Kirshi and colleagues (Kishi 2016) similarly conducted a systematic review to examine antipsychotics for treatment of delirium. The review also included both ICU and non-ICU participant populations in 15 studies. Four of the studies included were unpublished or in abstract form only; these were excluded from our review as well as the Neufeld review. The primary outcomes measure for Kirshi's review was response rate at the study end point, examining many different severity and global scales. They found antipsychotics were superior to placebo or nonantipsychotic drugs in this analysis of ICU and non-ICU studies in terms of response rate (RR 0.22, 95% CI 0.15 to 0.34,  $P < 0.00001$ ,  $I^2 = 0\%$ , three studies). When they performed a subgroup analysis using only ICU studies they found the pooled result was marginally superior to placebo or nonantipsychotic drugs (RR 0.25, 95% CI 0.06 to 1.02,  $p = 0.05$ ,  $N = 1$ ); using only non-ICU studies the result was the same as the pooled ICU and non-ICU studies with antipsychotics significantly superior to no antipsychotic (RR 0.22, 95% CI 0.15 to 0.34,  $P < 0.00001$ ,  $I^2 = 0\%$ , two studies). Similarly for the analysis of delirium severity, antipsychotics were significantly superior to no antipsychotic (SMD -1.27, 95% CI -2.44 to -0.11,  $P = 0.03$ ,  $I^2 = 93\%$ , two studies). For these analyses, we included two additional trials.

## AUTHORS' CONCLUSIONS

### Implications for practice

- Survey data indicates pharmacological interventions, such as antipsychotics, are often used to manage delirium symptoms in clinical practice. The 2010 NICE guidelines (NICE 2010) recommended clinicians should investigate and manage underlying or reversible causes of delirium. For patients that are distressed, verbal and nonverbal techniques should be used to manage symptoms; if these strategies are ineffective or insufficient, short-term (< 1 week) antipsychotic drug might be considered at the lowest effective dose.

- After updating this review, we caution clinicians to the fact that there is still insufficient evidence overall on this subject. We found no evidence to determine whether antipsychotics reduce delirium duration in hospitalised non-ICU patients (our primary objective). We found low-quality evidence that antipsychotics do not reduce delirium severity compared to nonantipsychotic drugs or placebo and low-quality evidence indicating there is no difference between typical and atypical antipsychotics. There is low-quality evidence that antipsychotics do not alter mortality or adverse event rates in delirious hospitalised patients.

### Implications for research

- The 2010 NICE guidelines (NICE 2010) recommended that a large RCT should be conducted to compare typical antipsychotics and atypical antipsychotics with placebo in hospitalised patients with delirium. The NICE guidelines also recommended the study outcomes of such a trial should include recovery from delirium (defined as complete response), the duration and severity of delirium (measured with a validated tool), as well as clinically important adverse events. Such a trial has been completed for palliative care participants (Agar 2016) but not for other important hospitalised non-ICU populations.

- Our search identified a number of delirium studies published in the last decade suggesting a growing interest in this subject. However, the majority of recent studies have focused on critically ill participants, still leaving us with insufficient poor quality data for hospitalised, non-critically ill participants (e.g. general medicine, surgery). Given the limited available evidence for this review, the 2010 NICE guideline recommendations calling for new research is still justified in 2018. Well designed controlled trials are urgently needed to address this population who are frequently managed with antipsychotics despite limited evidence. In particular, we need adequately powered trials that include a placebo group and factor in nonpharmacological delirium treatment strategies that have already been shown to be helpful in this population to clarify if an antipsychotic alters delirium outcomes. These trials should clearly standardise and describe the use of rescue interventions to manage agitation (e.g. benzodiazepines and physical restraints), as such interventions are known to be associated with delirium and can introduce bias.

- Our search revealed limited data on outcomes that we deemed important for patients, their families, and the clinical team. Future studies need to examine the effect of therapy on duration of delirium or time to complete resolution, length of hospital stay, and long-term outcomes, such as cognitive impairment. In addition, to improve comparison of results among trials there is a need for standardisation of research methods and outcomes reported, specifically duration of therapy and methods of evaluating response to delirium treatment. The Del-CORs (Development of core outcome sets for effectiveness trial of interventions to prevent and/or treat delirium) group (Rose 2017) is leading the development of international consensus on outcomes for trials of interventions to prevent and/or treat delirium for critically ill, acutely hospitalised participants, palliative care, and older adults. The recommendations from this group will be essential for future well designed delirium trials.

## ACKNOWLEDGEMENTS

We would like to especially thank Melanie Guenette, research coordinator, who played a pivotal role in protocol redevelopment, library and data management, and completion of the revised manuscript. We would also like to acknowledge Anna Noel-Storr, and Becky Skidmore, information specialists, for their assistance designing and executing the search strategy. We would like to thank our trainees, Anjuli Little and Barbara Sneyers, who assisted in the development of the search strategy and piloted the study data extraction forms. We thank Sue Marcus (Managing Editor) of the Cochrane Dementia Group. Lastly, we thank Neill Adhikari, Ingrid Egerod, Wesley Ely, Jose Morais (Canadian Geriatric Society), Doug Sellinger (Canadian Society of Hospital Pharmacists), Samir Sinha, Camilla Wong, and Lesley Wiesenfeld for their editorial advice during the preparation of our grant application.

## REFERENCES

### References to studies included in this review

#### Agar 2016 *{published data only}*

Agar M, Lawlor P, Quinn S, Draper B, Caplan G, Rowett D, et al. Efficacy of oral risperidone, haloperidol, or placebo for symptoms of delirium among patients in palliative care: a randomized clinical trial. *JAMA Internal Medicine* 2016; **177**(1):34–42.

#### Breitbart 1996 *{published data only}*

Breitbart W, Marotta R, Platt MM, Weisman H, Derevenco M, Grau C, et al. A double-blind trial of haloperidol, chlorpromazine, and lorazepam in the treatment of delirium in hospitalized AIDS patients. *American Journal of Psychiatry* 1996; **153**(2):231–7.

#### Grover 2011 *{published data only}*

Grover S, Kumar V, Chakrabarti S. Comparative efficacy study of haloperidol, olanzapine and risperidone in delirium. *Journal of Psychosomatic Research* 2011; **71**(4): 277–81.

#### Grover 2016 *{published data only}*

Grover S, Mahajan S, Chakrabarti S, Avasthi A. Comparative effectiveness of quetiapine and haloperidol in delirium: a single blind randomized controlled study. *World Journal of Psychiatry* 2016; **6**(3):365–71.

#### Han 2004 *{published data only}*

Han CS, Kim YK. A double-blind trial of risperidone and haloperidol for the treatment of delirium. *Psychosomatics* 2004; **45**(4):297–301.

#### Hu 2004 *{published data only}*

Hu H, Deng W, Yang H. A prospective random control study: comparison of olanzapine and haloperidol in senile delirium. *Chongqing Medical Journal* 2004; **8**(7):1234–7.

#### Lin 2008 *{published data only}*

Lin CJ, Sun FJ, Fang CK, Chen HW, Lai YL. An open trial comparing haloperidol with olanzapine for the treatment of delirium in palliative and hospice center cancer patients. *Journal of Internal Medicine of Taiwan* 2008; **19**:346–54.

#### Maneeton 2013 *{published data only}*

Maneeton B, Maneeton N, Srisurapanont M, Chittawatanarat K. Quetiapine versus haloperidol in the treatment of delirium: a double-blind, randomized, controlled trial. *Drug Design, Development and Therapy* 2013; **7**:657–67.

#### Tahir 2010 *{published data only}*

Tahir TA, Eeles E, Karapareddy V, Muthuvelu P, Chapple S, Phillips B, et al. A randomized controlled trial of quetiapine versus placebo in the treatment of delirium. *Journal of Psychosomatic Research* 2010; **69**(5):485–90.

### References to studies excluded from this review

#### Al Qadheeb 2016 *{published data only}*

Al-Qadheeb NS, Skrobik Y, Schumaker G, Pacheco MN, Roberts RJ, Ruthazer RR, et al. Randomized ICU trials do not demonstrate an association between interventions that reduce delirium duration and short-term mortality: a systematic review and meta-analysis. *Critical Care Medicine* 2014; **42**(6):1442–54.

#### Atalan 2013 *{published data only}*

Atalan N, Sevim ME, Akgun S, Fazligullari O, Basaran C. Morphine is a reasonable alternative to haloperidol in the treatment of postoperative hyperactive-type delirium after cardiac surgery. *Journal of Cardiothoracic and Vascular Anesthesia* 2013; **27**(5):933–8.

#### Bakri 2015 *{published data only}*

Bakri MH, Ismail EA, Ibrahim A. Comparison of dexmedetomidine or ondansetron with haloperidol for treatment of postoperative delirium in trauma patients admitted to intensive care unit: randomized controlled trial. *Anaesthesia, Pain & Intensive Care* 2015; **19**(2):118–23.

#### Devlin 2010 *{published data only}*

Devlin JW, Robert RJ, Fong JJ, Skrobik Y, Riker RR, Hill NS, et al. Efficacy and safety of quetiapine in critically ill patients with delirium: a prospective, multicenter,

- randomized, double-blind, placebo-controlled pilot study. *Critical Care Medicine* 2010;**38**(2):419–27.
- Girard 2010** {published data only}  
Girard TD, Pandharipande PP, Carson SS, Schmidt GA, Wright PE, Canonico AE, et al. Feasibility, efficacy, and safety of antipsychotics for intensive care unit delirium: the MIND randomized, placebo-controlled trial. *Critical Care Medicine* 2010;**38**(2):428–37.
- Hakim 2012** {published data only}  
Hakim SM, Othman AI, Naoum DO. Early treatment with risperidone for subsyndromal delirium after on-pump cardiac surgery in the elderly: a randomized trial. *Anesthesiology* 2012;**116**(5):987–97.
- Jung 2009** {published data only}  
Jung SW, Kim KS. A randomized controlled, pilot study of aripiprazole in the treatment of delirium. *European Neuropsychopharmacology* 2009;**19**(Supp 3):S553–4.
- Jung 2010** {published data only}  
Jung SW, Sakong JK, Lee JY, Choi YR, Suh HS. Comparison between effectiveness of quetiapine and risperidone for treatment of delirium in hospitalized patients. *International Journal of Neuropsychopharmacology* 2010;**13**:96.
- Kim 2010** {published data only}  
Kim SW, Yoo JA, Lee SY, Kim SY, Bae KY, Yang SJ, et al. Risperidone versus olanzapine for the treatment of patients with delirium. *Human Psychopharmacology* 2010;**25**(4): 298–302.
- Lee 2005** {published data only}  
Lee KU, Won WY, Lee HK, Kweon YS, Lee CT, Pae CU, et al. Amisulpride versus quetiapine for the treatment of delirium: a randomized, open prospective study. *International Clinical Psychopharmacology* 2005;**20**(6): e311–e314.
- Page 2013** {published data only}  
Page VJ, Ely EW, Gates S, Zhao XB, Alce T, Shintani A, et al. Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): a randomised, double-blind, placebo-controlled trial. *Lancet Respiratory Medicine* 2013;**1**(7):515–23.
- Reade 2009** {published data only}  
Reade MC, O'Sullivan K, Bates S, Goldsmith D, Ainslie WRTSJ, Bellomo R. Dexmedetomidine vs. haloperidol in delirious, agitated, intubated patients: a randomised open-label trial. *Critical Care* 2009;**13**(3):R75.
- Reade 2016** {published data only}  
Reade MC, Eastwood GM, Bellomo R, Bailey M, Bersten A, Cheung B, et al. Effect of dexmedetomidine added to standard care on ventilator-free time in patients with agitated delirium: a randomized clinical trial. *JAMA* 2016; **315**(14):1460–8.
- Sakong 2010** {published data only}  
Sakong JK, Jung SW, Kim JS, Koo BH. Comparison between effectiveness of aripiprazole and risperidone for treatment of delirium in hospitalized patients. *European Neuropsychopharmacology* 2010;**20**:S568–9.
- Skrobik 2014** {published data only}  
Skrobik Y, Bergeron N, Dumont M, Gottfried SB. Olanzapine vs haloperidol: treating delirium in a critical care setting. *Intensive Care Medicine* 2004;**30**(3):444–9.

## References to studies awaiting assessment

- Djokic 2008** {published data only}  
Djokic G, Zivkovic N, Pavicevic D, et al. Risperidone vs. haloperidol in treatment of delirium superimposed on dementia. *European Neuropsychopharmacology* 2008;**18** Suppl 4:S504–5.
- Jung Jin 2009** {published data only}  
Jung Jin K, Hyun Kook L, Chi Un P, Chang Uk L, In Ho P, Chul L. Comparison of intramuscular olanzapine and haloperidol for the treatment of delirium. *European Psychiatry* 2009;**24**:S1006.
- Lee 2013** {published data only}  
Lee J. Comparison of efficacy and side effects between aripiprazole and haloperidol in the treatment of delirium. *International Psychogeriatrics* 2013;**1**:S132–3.
- Nakamura 1997** {published data only}  
Nakamura J, Uchimura N, Yamada S, Nakazawa Y. Does plasma free-3-methoxy-4-hydroxyphenyl(ethylene)glycol increase in the delirious state? A comparison of the effects of mianserin and haloperidol on delirium. *International Clinical Psychopharmacology* 1997;**12**(3):147–52.

## References to ongoing studies

- NCT02345902** {published data only}  
NCT02345902. Treatment of hypoactive delirium and outcome measures. [clinicaltrials.gov/ct2/show/NCT02345902?term=NCT02345902&rank=1](https://clinicaltrials.gov/ct2/show/NCT02345902?term=NCT02345902&rank=1) (first received 26 January 2015).

## Additional references

- American Psychiatric Association 1999**  
American Psychiatric Association. Practice guidelines for the treatment of patients with delirium. *American Journal of Psychiatry* 1999;**156** Suppl:1–20.
- Barr 2013**  
Barr J, Fraser GL, Puntillo K, Ely EW, Gelinas C, Dasta JF, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Critical Care Medicine* 2013;**41**(1): 263–306.
- Boettger 2011a**  
Boettger SB, Breitbart W, Passik S. Haloperidol and risperidone in the treatment of delirium and its subtypes. *European Journal of Psychiatry* 2011;**25**(2):59–67.
- Boettger 2011b**  
Boettger S, Friedlander M, Breitbart W, Passik S. Aripiprazole and haloperidol in the treatment of delirium. *Australian and New Zealand Journal of Psychiatry* 2011;**45** (6):477–82.



**Breitbart 1997**

Breitbart W, Rosenfeld B, Roth A, Smith MJ, Cohen K, Passik S. The Memorial Delirium Assessment Scale. *Journal of Pain and Symptom Management* 1997;**13**(3):128–37.

**Breitbart 2002a**

Breitbart W, Gibson C, Tremblay A. The delirium experience: delirium recall and delirium-related distress in hospitalized patients with cancer, their spouses/caregivers, and their nurses. *Psychosomatics* 2002;**43**(3):183–94.

**Breitbart 2002b**

Breitbart W, Tremblay A, Gibson C. An open trial of olanzapine for the treatment of delirium in hospitalized cancer patients. *Psychosomatics* 2002;**43**(3):175–82.

**Briskman 2010**

Briskman I, Dubinski R, Barak Y. Treating delirium in a general hospital: a descriptive study of prescribing patterns and outcomes. *International Psychogeriatrics* 2010;**22**(2):328–31.

**British Geriatric Society 2006**

British Geriatric Society. Clinical guidelines for the prevention, diagnosis and management of delirium in older people in hospital. [www.bgs.org.uk/Publications/Clinical%20Guidelines/clinical.1-2\\_fulldelirium.htm](http://www.bgs.org.uk/Publications/Clinical%20Guidelines/clinical.1-2_fulldelirium.htm) (accessed 1 December 2014).

**Bruera 2009**

Bruera E, Bush SH, Willey J, Paraskevopoulos T, Li Z, Palmer JL, et al. Impact of delirium and recall on the level of distress in patients with advanced cancer and their family caregivers. *Cancer* 2009;**115**(9):2004–12.

**Burry 2015**

Burry L, Mehta S, Williamson DR, Hutton B, Ely EW, Adhikari NKJ, et al. Pharmacological interventions for the treatment of delirium in critically ill patients. *Cochrane Database of Systematic Reviews of Interventions* 2015, Issue 6. DOI: 10.1002/14651858.CD011749

**Buss 2007**

Buss MK, Vanderwerker LC, Inouye SK, Zhang B, Block SD, Prigerson HG. Associations between caregiver-perceived delirium in patients with cancer and generalized anxiety in their caregivers. *Journal of Palliative Medicine* 2007;**10**(5):1083–93.

**Buurman 2011**

Buurman BM, Hoogerduijn JG, De Haan RJ, Abu-Hanna A, Lagaay AM, Verhaar HJ, et al. Geriatric conditions in acutely hospitalized older patients: prevalence and one-year survival and functional decline. *PLOS One* 2011;**6**(11):e26951.

**Carnes 2003**

Carnes M, Howell T, Rosenberg M, Francis J, Hildebrand C, Knuppel J. Physicians vary in approaches to the clinical management of delirium. *Journal of the American Geriatrics Society* 2003;**51**(2):234–9.

**CEHSE 2006**

Clinical Epidemiology and Health Service Evaluation Unit, Melbourne Health and the Australian Health Ministers'

Health Care of Older Australians Standing Committee. Clinical Practice Guidelines for the Management of Delirium in Older People. [www.health.vic.gov.au/acute-agedcare/](http://www.health.vic.gov.au/acute-agedcare/) (accessed 1 February 2015).

**Cerejeira 2010**

Cerejeira J, Firmino HC, Vaz-Serra A, Mukaetova-Ladinska EB. The neuroinflammatory hypothesis of delirium. *Acta Neuropathologica* 2010;**119**(6):737–54.

**Cohen 2009**

Cohen MZ, Pace EA, Kaur G, Bruera E. Delirium in advanced cancer leading to distress in patients and family caregivers. *Journal of Palliative Care* 2009;**25**(3):164–71.

**Cole 2009**

Cole MG, Ciampi A, Belzile E, Zhong L. Persistent delirium in older hospital patients: a systematic review of frequency and prognosis. *Age & Ageing* 2009;**38**(1):19–26.

**DeMets 1987**

DeMets DL. Methods for combining randomized clinical trials. *Statistics in Medicine* 1987;**6**(3):341–50.

**Devlin 2011**

Devlin JW, Skrobik Y, Riker RR, Hinderleider E, Roberts RJ, Fong JJ, et al. Impact of quetiapine on resolution of individual delirium symptoms in critically ill patients with delirium: a post-hoc analysis of a double-blind, randomized, placebo-controlled study. *Critical Care* 2011;**15**(5):R215.

**DSM-IV 1994**

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. American Psychiatric Association, 1994.

**DSM-IV-TR 2000**

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th Edition. Washington: American Psychiatric Association, 2000.

**DSM-V 2013**

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th Edition. Arlington: American Psychiatric Association, 2013.

**Egger 1997**

Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**:629–34.

**Endnotes [Computer program]**

Thomson Reuters. EndNote (Endnote Version X6). Calsbad, CA, USA: Thomson Reuters, 2012.

**Flacker 1999**

Flacker JM, Lipsitz LA. Neural mechanisms of delirium: current hypotheses and evolving concepts. *Journals of Gerontology. Series A: Biological Sciences and Medical Sciences* 1999;**54**(6):B239–46.

**Fosnight 2011**

Fosnight S. Delirium in the elderly. In: Richardson M, Chant C, Chessman KH, Finks SW, Hemstreet BA, Hume AL, et al editor(s). *Pharmacotherapy Self-Assessment Program*. 7th Edition. Lenexa: American College of Clinical Pharmacy, 2011:73–95.

**Gaudreau 2005**

Gaudreau JD, Gagnon P. Psychotogenic drugs and delirium pathogenesis: the central role of the thalamus. *Medical Hypotheses* 2005;**64**(3):471–5.

**Gill 2007**

Gill SS, Bronskill SE, Normand SL, Anderson GM, Sykora K, Lam K, et al. Antipsychotic drug use and mortality in older adults with dementia. *Annals of Internal Medicine* 2007;**146**(11):775–86.

**Gillick 1982**

Gillick MR, Serrell NA, Gillick LS. Adverse consequences of hospitalization in the elderly. *Social Science and Medicine* 1982;**16**(10):1033–8.

**Gleason 2003**

Gleason OC. Delirium. *American Family Physician* 2003;**67**(5):1027–34.

**GRADEpro GDT 2015 [Computer program]**

Evidence Prime, Inc. GRADEpro Guideline Development Tool. Version (accessed prior to 17 May 2018). Hamilton (ON): McMaster University, 2015. [gradepro.org]

**Guyatt 2008**

Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;**336**(7650):924–6.

**Han 2010**

Han JH, Shintani A, Eden S, Morandi A, Solberg LM, Schnelle J, et al. Delirium in the emergency department: an independent predictor of death within 6 months. *Annals of Emergency Medicine* 2010;**56**(3):244–52.

**Hatta 2014**

Hatta K, Kishi Y, Wada K, Odawara T, Takeuchi T, Shiganami T, et al. Antipsychotics for delirium in the general hospital setting in consecutive 2453 inpatients: a prospective observational study. *International Journal of Geriatric Psychiatry* 2014;**29**(3):253–62.

**Higgins 2003**

Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**(7414):557–60.

**Higgins 2011**

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

**Hsieh 2008**

Hsieh TT, Fong TG, Marcantonio ER, Inouye SK. Cholinergic deficiency hypothesis in delirium: a synthesis of current evidence. *Journals of Gerontology: Series A* 2008;**63**(7):764–72.

**Hua 2006**

Hua H, Wei D, Hui Y, Yu L. Olanzapine and haloperidol for senile delirium: a randomized controlled observation. *Chinese Journal of Clinical Rehabilitation* 2006;**10**(42):188–90.

**IHI 2014**

Institute for Healthcare Improvement. Sedation, delirium, and mobility. [www.ihl.org/Pages/default.aspx](http://www.ihl.org/Pages/default.aspx) (accessed 3 February 2015).

**Inouye 1990**

Inouye SK, Van Dyck CH, Alessi CA, Balkin S, Siegel AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Annals of Internal Medicine* 1990;**113**(12):941–8.

**Inouye 1996**

Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. *Journal of the American Medical Association* 1996;**275**(11):852–7.

**Inouye 1998**

Inouye SK, Rushing JT, Foreman MD, Palmer RM, Pompei P. Does delirium contribute to poor hospital outcomes? A three-site epidemiologic study. *Journal of General Internal Medicine* 1998;**13**(4):234–42.

**Inouye 1999**

Inouye SK, Schlesinger MJ, Lydon TJ. Delirium: a symptom of how hospital care is failing older persons and a window to improve quality of hospital care. *American Journal of Medicine* 1999;**106**(5):565–73.

**Inouye 2001**

Inouye SK, Foreman MD, Mion LC, Katz KH, Cooney LM Jr. Nurses' recognition of delirium and its symptoms: comparison of nurse and researcher ratings. *Archives of Internal Medicine* 2001;**161**(20):2467–73.

**Inouye 2006a**

Inouye SK. Delirium in older persons. *New England Journal of Medicine* 2006;**354**(11):1157–65.

**Inouye 2006b**

Inouye SK, Baker DI, Fugal P, Bradley EH, Project HD. Dissemination of the hospital elder life program: implementation, adaptation, and successes. *Journal of the American Geriatrics Society* 2006;**54**(10):1492–9.

**Inouye 2014**

Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *Lancet* 2014;**383**(9920):911–22.

**Ito 2007**

Ito T, Okubo Y. Aripiprazole in the treatment of hypoactive subtype of delirium with terminal cancer patients. Proceedings of the Academy of Psychosomatic Medicine. 2007:31.

**Kakuma 2003**

Kakuma R, Du Fort GG, Arseneault L, Perrault A, Platt RW, Monette J, et al. Delirium in older emergency department patients discharged home: effect on survival. *Journal of the American Geriatric Society* 2003;**51**(4):443–50.

**Kim 2003**

Kim KY, Bader GM, Kotlyar V, Gropper D. Treatment of delirium in older adults with quetiapine. *Journal of Geriatric Psychiatry and Neurology* 2003;**16**(1):29–31.

**Kishi 2016**

Kishi T, Hirota T, Matsunaga S, Iwata N. Antipsychotic medications for the treatment of delirium: a systematic review and meta-analysis of randomised controlled trials. *J Neurology, Neurosurgery, & Psychiatry* 2016;**87**:767–74.

**Leonard 2015**

Leonard M, Adamis D, Saunders J, Trzepacz P, Meagher D. A longitudinal study of delirium phenomenology indicates widespread neural dysfunction. *Palliative and Supportive Care* 2015;**13**(2):187–96.

**Leslie 2005**

Leslie DL, Zhang Y, Holford TR, Bogardus ST, Leo-Summers LS, Inouye SK. Premature death associated with delirium at 1-year follow-up. *Archives of Internal Medicine* 2005;**165**(14):1657–62.

**Leslie 2008**

Leslie DL, Marcantonio ER, Zhang Y, Leo-Summers L, Inouye SK. One-year health care costs associated with delirium in the elderly population. *Archives of Internal Medicine* 2008;**168**(1):27–32.

**Levkoff 1992**

Levkoff SE, Evans DA, Liptzin B, Cleary PD, Lipsitz LA, Wetle TT, et al. Delirium. The occurrence and persistence of symptoms among elderly hospitalized patients. *Archives of Internal Medicine* 1992;**152**(2):334–40.

**Lundstrom 2005**

Lundstrom M, Edlund A, Karlsson S, Brannstrom B, Bucht G, Gustafson Y. A multifactorial intervention program reduces the duration of delirium, length of hospitalization, and mortality in delirious patients. *Journal of the American Geriatrics Society* 2005;**53**(4):622–8.

**MacLulich 2013**

MacLulich AM, Anand A, Davis DH, Jackson T, Barugh AJ, Hall RJ, et al. New horizons in the pathogenesis, assessment and management of delirium. *Age & Ageing* 2013;**42**(6):667–74.

**McCusker 2001**

McCusker J, Cole M, Dendukuri N, Belzile E, Primeau F. Delirium in older medical inpatients and subsequent cognitive and functional status: a prospective study. *Canadian Medical Association Journal* 2001;**165**(5):575–83.

**McCusker 2002**

McCusker J, Cole M, Abrahamowicz M, Primeau F, Belzile E. Delirium predicts 12-month mortality. *Archives of Internal Medicine* 2002;**162**(4):457–63.

**McCusker 2003**

McCusker J, Cole M, Dendukuri N, Han L, Belzile E. The course of delirium in older medical inpatients: a prospective study. *Journal of General Internal Medicine* 2003;**18**(9):696–704.

**Meagher 2010**

Meagher DJ. Impact of an educational workshop upon attitudes towards pharmacotherapy for delirium. *International Psychogeriatrics* 2010;**22**(6):938–46.

**Meagher 2012**

Meagher D, Adamis D, Trzepacz P, Leonard M. Features of subsyndromal and persistent delirium. *British Journal of Psychiatry* 2012;**200**(1):37–44.

**Mittal 2011**

Mittal V, Kurup L, Williamson D, Muralee S, Tampi RR. Risk of cerebrovascular adverse events and death in elderly patients with dementia when treated with antipsychotic medications: a literature review of evidence. *American Journal of Alzheimer's Disease and Other Dementias* 2011;**26**(1):10–28.

**Morita 2004**

Morita T, Hirai K, Sakaguchi Y, Tsuneto S, Shima Y. Family-perceived distress from delirium-related symptoms of terminally ill cancer patients. *Psychosomatics* 2004;**45**(2):107–13.

**Neelon 1996**

Neelon VJ, Champagne MT, Carlson JR, Funk SG. The NEECHAM Confusion Scale: construction, validation, and clinical testing. *Nursing Research* 1996;**45**(6):324–30.

**Neufeld 2016**

Neufeld KJ, Yue J, Robinson TN, Inouye SK, Needham DM. Antipsychotic medication for prevention and treatment of delirium in hospitalized adults: a systematic review and meta-analysis. *Journal of the American Geriatrics Society* 2016;**64**(4):705–14.

**NICE 2010**

National Institute for Health and Clinical Excellence. Delirium: Diagnosis, Prevention, and Management (Clinical Guideline 103). [www.nice.org.uk/CG103](http://www.nice.org.uk/CG103) (accessed 4 January 2015).

**OECD 2012**

Organization for Economic Co-operation and Development. OECD Health Data. [www.oecd.org/health/](http://www.oecd.org/health/) (accessed 3 December 2014).

**Parellada 2004**

Parellada E, Baeza I, De Pablo J, Martinez G. Risperidone in the treatment of patients with delirium. *Journal of Clinical Psychiatry* 2004;**65**(3):348–53.

**Partridge 2013**

Partridge JS, Martin FC, Harari D, Dhesi JK. The delirium experience: what is the effect on patients, relatives and staff and what can be done to modify this?. *International Journal of Geriatric Psychiatry* 2013;**28**(8):804–12.

**Pitkala 2005**

Pitkala KH, Laurila JV, Strandberg TE, Tilvis RS. Prognostic significance of delirium in frail older people. *Dementia and Geriatric Cognitive Disorders* 2005;**19**(2-3):158–63.

**Platt 1994**

Platt MM, Breitbart W, Smith M, Marotta R, Weisman H, Jacobsen PB. Efficacy of neuroleptics for hypoactive delirium. *Journal of Neuropsychiatry and Clinical Neuroscience* 1994;**6**(1):66–7.

**Pompei 1994**

Pompei P, Foreman M, Rudberg MA, Inouye SK, Braund V, Cassel CK. Delirium in hospitalized older persons: outcomes and predictors. *Journal of the American Geriatrics Society* 1994;**42**(8):809–15.

**Ray 2009**

Ray WA, Chung CP, Murray KT, Hall K, Stein CM. Atypical antipsychotic drugs and the risk of sudden cardiac death. *New England Journal of Medicine* 2009;**360**(3):225–35.

**RCP 2006**

Royal College of Psychiatrists. The prevention, diagnosis and management of delirium in older people (National Guidelines). [www.rcplondon.ac.uk/sites/default/files/concise-delirium-2006.pdf](http://www.rcplondon.ac.uk/sites/default/files/concise-delirium-2006.pdf) (accessed 11 December 2014).

**RevMan 2014 [Computer program]**

Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager 5 (RevMan 5). Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

**Rizzo 2001**

Rizzo JA, Bogardus ST Jr, Leo-Summers L, Williams CS, Acampora D, Inouye SK. Multicomponent targeted intervention to prevent delirium in hospitalized older patients: what is the economic value?. *Medical Care* 2001;**39**(7):740–52.

**Rolfson 2002**

Rolfson D. The causes of delirium. In: Lindsay JRK, Macdonald A editor(s). *Delirium in Old Age*. Oxford: Oxford University Press, 2002:101–22.

**Rose 2017**

Rose L, Agar M, Burry LD, Campbell N, Clarke M, Lee J, et al. Development of core outcome sets for effectiveness trials of interventions to prevent and/or treat delirium (Del-CORs): study protocol. *BMJ Open* 2017;**7**:e016371. [PUBMED: 28928181]

**Rothschild 2000**

Rothschild JM, Bates DW, Leape LL. Preventable medical injuries in older patients. *Archives of Internal Medicine* 2000;**160**(18):2717–28.

**Rudolph 2011**

Rudolph JL, Marcantonio ER. Review articles: postoperative delirium: acute change with long-term implications. *Anesthesia and Analgesia* 2011;**112**(5):1202–11.

**Safer Healthcare Now 2005**

Safer Healthcare Now!. Prevention and management of delirium. [www.saferhealthcarenow.ca/EN/Interventions/DeliriumPrevention/Pages/default.aspx](http://www.saferhealthcarenow.ca/EN/Interventions/DeliriumPrevention/Pages/default.aspx) (accessed 30 November 2014).

**Salluh 2010**

Salluh JL, Soares M, Teles JM, Ceraso D, Raimondi N, Nava VS, et al. Delirium epidemiology in critical care (DECCA): an international study. *Critical Care* 2010;**14**(6):R10.

**Sasaki 2003**

Sasaki Y, Matsuyama T, Inoue S, Sunami T, Inoue T, Denda K, et al. A prospective, open-label, flexible-dose study of quetiapine in the treatment of delirium. *Journal of Clinical Psychiatry* 2003;**64**(11):1316–21.

**Schneider 2005**

Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. *Journal of the American Medical Association* 2005;**294**(15):1934–43.

**Thomas 2008**

Thomas C, Hestermann U, Kopitz J, Plaschke K, Oster P, Driessen M, et al. Serum anticholinergic activity and cerebral cholinergic dysfunction: an EEG study in frail elderly with and without delirium. *BMC Neuroscience* 2008;**9**:86.

**Traube 2014**

Traube C, Silver G, Kearney J, Patel A, Atkinson TM, Yoon MJ, et al. Cornell Assessment of Pediatric Delirium: a valid, rapid, observational tool for screening delirium in the PICU. *Critical Care Medicine* 2014;**42**(3):656–63.

**Trzepacz 1988**

Trzepacz PT, Baker RW, Greenhouse J. A symptom rating scale for delirium. *Psychiatry Research* 1988;**23**(1):89–97.

**Trzepacz 1999**

Trzepacz PT. Update on the neuropathogenesis of delirium. *Dementia and Geriatric Cognitive Disorders* 1999;**10**(5):330–4.

**Trzepacz 2000**

Trzepacz PT. Is there a final common neural pathway in delirium? Focus on acetylcholine and dopamine. *Seminars in Clinical Neuropsychiatry* 2000;**5**(2):132–48.

**Trzepacz 2001**

Trzepacz PT, Mittal D, Torres R, Kanary K, Norton J, Jimerson N. Validation of the Delirium Rating Scale-revised-98: comparison with the delirium rating scale and the cognitive test for delirium. *Journal of Neuropsychiatry and Clinical Neurosciences* 2001;**13**(2):229–42.

**Van der Cammen 2006**

Van der Cammen TJ, Tiemeier H, Engelhart MJ, Fekkes D. Abnormal neurotransmitter metabolite levels in Alzheimer patients with a delirium. *International Journal of Geriatric Psychiatry* 2006;**21**(9):838–43.

**Vasilevskis 2012**

Vasilevskis EE, Han JH, Hughes CG, Ely EW. Epidemiology and risk factors for delirium across hospital settings. *Best Practice & Research Clinical Anaesthesiology* 2012;**26**:277–87.

**Wang 2005**

Wang PS, Schneeweiss S, Avorn J, Fischer MA, Mogun H, Solomon DH, et al. Risk of death in elderly users of conventional vs. atypical antipsychotic medications. *New England Journal of Medicine* 2005;**353**(22):2335–41.

**Watt 2013**

Watt DBD, Koziol LF. Delirium. In: Noggle C, Dean R editor(s). *The Neuropsychology of Psychopathology*. New York: Springer Publishing Company, 2013:425–40.

**WHO 2012**

WHO Regional Office for Europe, World Health Organization. European hospital morbidity database. [data.euro.who.int/hmdb/index.php](http://data.euro.who.int/hmdb/index.php) (accessed 16 October 2014).

**Witlox 2010**

Witlox J, Eurelings LS, De Jonghe JF, Kalisvaart KJ, Eikelenboom P, Van Gool WA. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization,

and dementia: a meta-analysis. *Journal of the American Medical Association* 2010;**304**(4):443–51.

**Young 1997**

Young BK, Camicioli R, Ganzini L. Neuropsychiatric adverse effects of antiparkinsonian drugs. Characteristics, evaluation and treatment. *Drugs & Aging* 1997;**10**(5): 367–83.

**References to other published versions of this review****Loneragan 2007**

Loneragan E, Britton AM, Luxenberg J. Antipsychotics for delirium. *Cochrane Database of Systematic Reviews* 2007, Issue 2. DOI: 10.1002/14651858.CD005594.pub2

\* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies [ordered by study ID]

Agar 2016

Methods	Double-blind, randomised trial comparing risperidone, haloperidol, and placebo on targeting symptoms of delirium
Participants	<p>Location: Study took place in 11 inpatient hospice or palliative care services in Australia.</p> <p>Inclusion: Participants included adult patients receiving hospice or palliative care with advanced, progressive disease that was no longer curable who required inpatient care by a specialist palliative care team. Participants were required to speak English and be able to swallow liquids. Participants needed to meet the following 3 criteria: delirium diagnosis via 1) DSM-IV-TR criteria, 2) Memorial Delirium Assessment Scale (MDAS) score of 7 or more, and 3) presence of the target symptoms of delirium associated with distress, defined as a delirium symptoms score of 1 or more (sum of the scores from items 2 (inappropriate behaviour), 3 (inappropriate communication), and 4 (illusions and hallucinations) on the Nursing Delirium Screening Scale (NuDESC) (severity range, 0 to 6)).</p> <p>Exclusion: delirium due to substance withdrawal, history of neuroleptic malignant syndrome or previous adverse reaction to an antipsychotic drug, regular use of antipsychotic drugs within 48 hours of the study, extrapyramidal disorders, prolonged QT interval, clinician-predicted survival of 7 days or fewer, cerebrovascular accident or seizure in the prior 30 days, and pregnancy or breastfeeding. Subjects included: 247 adult participants (N = 82 risperidone, mean age <math>74.5 \pm 10.6</math> years, 57/82 (69%) male, N = 81 haloperidol, mean age <math>76.5 \pm 8.2</math> years, 48/81 (59%) male, N = 84 placebo, mean age <math>73.8 \pm 10.7</math> years, 57/84 (68%) male)</p>
Interventions	<p>Each study drug arm: 1) Participants <math>\leq 65</math> years received a 0.5 mg loading dose of study drug administered with the first dose of 0.5 mg, then 0.5 mg maintenance doses every 12 hours. Doses could be titrated by 0.25 mg on day 1 and by 0.5 mg thereafter to a maximum dose of 4 mg/d. 2) For participants <math>&gt; 65</math> years, the loading, initial, and maximum doses of the study drug were halved. The placebo solution was titrated similarly using matching volumes of solution for each dose level. Doses were increased if the sum of NuDESC scores for items 2, 3, and 4 was 1 or more at the most recent assessment. Participants were observed daily, with NuDESC scores measured every 8 hours by trained nurses. Dose reduction of the prior dose could occur for adverse effects, resolution of delirium (MDAS score of <math>&lt; 7</math> for 48 hours), or resolution of symptoms (all NuDESC item scores <math>&lt; 1</math> for 48 hours). Treatment duration was 72 hours, with the last assessment done 12 hours after the sixth dose</p> <p>Study drug was discontinued if adverse effects became unacceptable, the treating clinician deemed the treatment ineffective, or at onset of dysphagia. Maintenance of blinded study medication was optional for an additional 48 hours if a partial response occurred or to taper the dose with resolution of symptoms. All participants received individualised treatment plans, including treatment of reversible precipitants, where clinically indicated, and nonpharmacologic measures, as appropriate. Rescue drug: Subcutaneous midazolam 2.5 mg every 2 hours PRN was available when participants in any group scored 2 on the NuDESC item for inappropriate behaviour or illusions and hallucinations, and were deemed to require immediate intervention for safety or distress. Intravenous benztropine mesylate (1 to 2 mg) could be administered for serious extrapyramidal adverse effects</p>

Outcomes	Clinical (day 3): 1) Average of last 2 delirium symptom scores on day 3, using the baseline score (average of the eligibility delirium symptom score and the score before the first dose of the study drug) as a covariate, 2) Daily MDAS score, 3) Lowest delirium symptoms score, 4) Daily use of midazolam (rescue drug), 5) Sedation, assessed by the Richmond Agitation-Sedation Scale, 6) Survival (measured at day 3 and also median survival (days)) . Adverse effects: 1) Extrapyramidal symptoms, assessed by the Extrapyramidal Symptom Rating Scale, 2) National Cancer Institute Common Terminology Criteria for Adverse Events	
Notes	Study was funded by the Australian Government’s Department of Health under the National Palliative Care Strategy. Individual site funding was supplemented by grant NHMRC 480476 from the National Health and Medical Research Council, Australia. The trial was registered (ACTRN12607000562471). Baseline covariates collected included: prior cognitive impairment (all cause), Informant Questionnaire on Cognitive Decline in the Elderly score, comorbidity burden (Cumulative Illness Rating Scale score) , vision or hearing impairment, daily oral morphine and diazepam equivalents, and the Australia-modified Karnofsky Performance Status score	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Site randomisation schedules generated using random number tables at an independent and blinded central registry. Participants were randomised in blocks of 6 by site in a 1:1:1 ratio
Allocation concealment (selection bias)	Low risk	Sealed opaque envelopes were used. Site clinical trial pharmacists not otherwise involved in patient care opened treatment schedules to prepare study drug
Blinding (performance bias and detection bias) All outcomes	Low risk	Double-blinded study - both participants and investigators were masked to treatment groups
Incomplete outcome data (attrition bias) All outcomes	Low risk	Intention-to-treat basis. Missing scores imputed using multiple imputation, drawing 50 resamples
Selective reporting (reporting bias)	Low risk	Outcomes in methods matched those reported in results. Trial protocol was pre-registered
Other bias	Low risk	All participants were permitted pain medication, rescue benzodiazepine, and given similar nonpharmacological interventions.

	Power calculations presented
<b>Breitbart 1996</b>	
Methods	Double-blind, randomised trial comparing haloperidol, chlorpromazine, and lorazepam in the treatment of delirium
Participants	<p>Location: Study took place in a single general medicine unit of one hospital in the United States. Inclusion: Medically hospitalised adults who met the case definition for AIDS and who were undergoing treatment for AIDS-related medical problems at a single hospital were approached for participation. They recruited and consented participants prior to the episode of delirium. Participants were followed prospectively and not randomised to study drug unless they became delirious. Exclusion: AIDS-related dementia where participants could not give informed consent, patients expected to die within 24 hours, known hypersensitivity to study drugs, history of neuroleptic malignant syndrome, concurrent need for treatment with neuroleptic drugs, seizure disorder, current systemic chemotherapy for Kaposi's sarcoma, withdrawal syndrome, current/past diagnosis for schizophrenia, schizoaffective disorder, or bipolar disorder</p> <p>Subjects included 30 adult participants (N = 11 haloperidol, N = 13 chlorpromazine, N = 6 lorazepam, mean age of entire study population <math>39.2 \pm 8.8</math> years, 23/30 (77%) male) hospitalised for AIDS-related medical problems and diagnosed with delirium (DSM-III criteria and Delirium Rating Scale (DRS) total score <math>\geq 13</math>)</p>
Interventions	<p>The study did not include a placebo group. The authors believed withholding medication from agitated participants could pose a risk to patients and staff, hence they did not use a placebo group. They viewed lorazepam as a placebo. Study drug: Participants were randomised to one of three groups by pharmacy personnel. Groups were: haloperidol, chlorpromazine, and lorazepam. Subjects were started on the lowest dose of their respective study drug, administered either orally or intramuscularly and according to an a priori established increasing titration schedule consisting of 9 levels of dosing (table 1 in manuscript). Haloperidol was started with 0.25 mg oral/0.125 mg intramuscular, chlorpromazine at 10 mg oral/5 mg intramuscular, and lorazepam at 0.5 mg oral/0.20 mg intramuscular. Each subject was evaluated hourly using the DRS. If, after each hourly evaluation, the participant's DRS score remained <math>\geq 13</math>, the next level dose of study drug was administered. After stabilisation (i.e. participant calm, asleep, not hallucinating, and <math>DRS \leq 12</math>), a maintenance dose equal to one-half of the first 24-hour dose requirement was begun, given in a twice-daily regimen from day 2 of the study until a maximum of six days of treatment. Midway through the study, the participants in one group developed treatment-limiting adverse side effects as per the manuscript. All participants were in the lorazepam group. From that point forward, no further participants were randomised to the lorazepam group. Rescue drugs: No rescue drugs permitted (additional details provided by author)</p>
Outcomes	<p>Outcomes (at end of study drug, day 6):</p> <ol style="list-style-type: none"> <li>1. Mean drug doses administered in first 24 hours of treatment,</li> <li>2. Average maintenance doses of study drug,</li> <li>3. DRS score, change from baseline to day 2, and day 2 to day 6,</li> <li>4. Mini-Mental State score, change from baseline to day 2, and day 2 to day 6,</li> <li>5. Karnofsky Performance Status,</li> <li>6. Medical Status Profile.</li> </ol> <p>Adverse effects: 1) Extrapyramidal symptoms, assessed by the Extrapyramidal Symptom Rating Scale, 2. Side Effects</p>



**Breitbart 1996** (Continued)

	and Symptom Checklist	
Notes	Study supported by the National Institute of Mental Health grant MH-45664	
<i>Risk of bias</i>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation table (additional details provided by author)
Allocation concealment (selection bias)	Low risk	Pharmacist not involved in the study patient care indicated which study drug was to be used based on the random number table
Blinding (performance bias and detection bias) All outcomes	Low risk	Double-blinded study.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Lorazepam arm discontinued early due to adverse events, but data used in analysis
Selective reporting (reporting bias)	Unclear risk	Outcomes in methods matched those reported in results. But protocol not published to confirm all outcomes were reported as planned
Other bias	Unclear risk	No rescue drugs permitted (additional details provided by author). Also, midway through the study, the participants in one group developed treatment-limiting adverse side effects as per the manuscript. All participants were in the lorazepam group. From that point forward, no further participants were randomised to the lorazepam group Note: Sample size/power calculation not reported in the manuscript

**Grover 2011**

Methods	Single-blind, randomised trial comparing haloperidol, risperidone, and olanzapine in the treatment of delirium
Participants	Location: Conducted in single hospital in India. Inclusion: Consecutive participants with delirium referred to the consultation-liaison psychiatry team were eligible for the study. To be included in the study, participants had to have a confirmed diagnosis

	of delirium and > 18 years of age. Exclusion: Participants with delirium secondary to alcohol or benzodiazepine withdrawal, those with dementia, those unresponsive to verbal or physical stimulus, those suffering terminal illness, and those with a comorbid psychotic/mood disorder, profound hearing or visual loss, aphasia, Parkinson's disease, history of neuroleptic malignant syndrome, prolonged QTc interval, past history of hypersensitivity to any of the study drugs. Participants included 64 adult (> 18 years) medical and surgical patients (N = 20 haloperidol, mean age 44.09 ± 16.84 years, 12/20 (60%) male, N = 21 risperidone, mean age 45.39 ± 19.18 years, 12/21 (57%) male, N = 23 olanzapine, mean age 46.5 ± 14.51 years, 21/23 (91%) males) diagnosed with delirium (CAM and DRS-R-98)
Interventions	There were three study groups: 1) Haloperidol: flexible dose ranging from 0.25 to 10 mg/day; 2) Risperidone: flexible dose ranging from 0.25 to 4 mg/day; and 3) Olanzapine: flexible dose ranging from 1.25 to 20 mg/day. Study drug was administered for 6 days and for all subjects, family members told to follow behavioural management (i. e. providing optimal level of environmental stimulation, reducing sensory impairments, making environment more familiar, providing environmental cues that facilitate orientation, and providing reassurance and information concerning delirium so as to reduce fear or demoralisation). Delirium screening occurred daily. For all participants, the etiological causes identified for delirium were treated with appropriate measures. Any medication that can cause delirium and/or was not essential for the care of the participant was discontinued. Rescue drugs: For the haloperidol and olanzapine groups, whenever rescue medication was required (e.g. severe agitation), the same drug was used in the injectable form. For the risperidone group, injectable lorazepam or haloperidol was used as rescue medication as risperidone not available in injectable form. The dose of rescue medication was titrated after daily clinical assessment; however, if the participant was agitated, titration was done more frequently
Outcomes	Outcomes (daily for 6 days by blinded investigator): 1. DRS-R-98 score, 2. Mini Mental Status Examination score. Adverse effects: 1. Simpson Angus Scale for side effects, 2. Abnormal Involuntary Movement Scale, 3. Udvalg for Kliniske Undersogelser score side effect rating scale
Notes	Study funded by Institute Research Fund. Protocol not published

***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated to be randomised but no details provided. It is likely that it was done
Allocation concealment (selection bias)	Low risk	Randomisation and dose adjustments were carried out by one study investigator, however, assessments were blinded
Blinding (performance bias and detection bias) All outcomes	Low risk	Single-blinded study. However, all assessments were carried out by a single investigator (different from the one who performed

**Grover 2011** (Continued)

		the randomisation and dose adjustments) who was blinded to study drug allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Of the 74 participants consented, 64 completed the study. Six participants could not be assessed at least once during the study (due to worsened clinical status) and four left hospital against medical advice
Selective reporting (reporting bias)	Unclear risk	Outcomes in methods matched those reported in results. Trial protocol not published so unable to confirm all outcomes were reported as planned
Other bias	Unclear risk	For both groups, etiological causes of delirium were addressed and nonessential medications or medications associated with delirium were discontinued. One group (i.e. risperidone) received lorazepam or haloperidol as injectable risperidone was not available. However, haloperidol and olanzapine groups received the same drug they were assigned to for rescue. Referral bias: participants who were referred to the consultation-liaison psychiatry team were eligible for the study. It is unknown if all participants with suspected delirium are routinely referred to psychiatry in this hospital Note: Sample size/power calculation not reported.

**Grover 2016**

Methods	Single-blind, randomised controlled trial of quetiapine and haloperidol for the treatment of delirium
Participants	Location: Study conducted in single hospital in India. Inclusion: Consecutive patients with delirium referred to the consultation-liaison psychiatry team were eligible for the study. Only patients who fulfilled a diagnosis of delirium based on DSM-IV and > 18 years could be included in the study. Exclusion: delirium due to alcohol or benzodiazepine withdrawal, poisoning, overdoses, dementia, those unresponsive to verbal or physical stimulus, history of aphasia, profound hearing or visual loss, those with QTc prolongation, past history of hypersensitivity to the study drugs, history of neuroleptic malignant syndrome, Parkinson's disease, psychotic or mood disorders, and terminal illness. Participants included 63 adult (> 18 years) medical and surgical patients (N = 31 quetiapine, mean age 48.51 ± 19.75 years, 21/31 (68%) male, N = 32 haloperidol, mean age 44.4 ± 16.76 years, 28/32 (88%) male) diagnosed with delirium (DSM-IV criteria)

Interventions	No placebo group. The study compared: 1) Haloperidol: flexible dose ranging from 0.25 to 10 mg/day and 2) Quetiapine: flexible dose ranging from 12.5 to 75 mg/day. Study drug was adjusted daily as per the clinical judgement of treating physician who was blinded to assignment. Study drug was administered for 6 days. For all subjects, caregivers advised to provide optimal level of environmental stimulation, avoid sensory impairments of the participant, and make the environment familiar to the participant by ensuring proper environmental cues that could facilitate orientation. Delirium screening occurred daily. Rescue drugs: Benzodiazepines were not permitted. Use of other drugs to manage severe agitation not reported	
Outcomes	Outcomes (at end of study drug, day 6): 1. DRS-R-98 score, 2. Mini Mental Status Examination score, 3. Average dose of study drug, 4. Delirium response rates (DRS-R-98 < 10), 5. Delirium resolution rates (DRS-R-98 score of 0). Adverse effects: None included as an outcome or reported	
Notes	Protocol not published in advance.	
<i><b>Risk of bias</b></i>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	Randomisation was done based on a computer-generated randomisation table, which was done prior to study start
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Low risk	Single-blinded study, however the investigator responsible for randomisation and drug titration was different from the one who conducted the outcome assessments (blinded clinical assessment)
Incomplete outcome data (attrition bias) All outcomes	High risk	Seven participants not included in the analysis. Two participants in each group were not available for assessment after the first 1 to 2 study days because they left against medical advice. One participant in the quetiapine group received injectable haloperidol for symptom management on study day 2, and was excluded. One participant from each group could not be started on the assigned medication due to medical deterioration
Selective reporting (reporting bias)	Unclear risk	Outcomes in methods matched those reported in results. Trial protocol not published so unable to confirm all outcomes

		were reported as planned
Other bias	Unclear risk	<p>Manuscript source reported as 'invited manuscript.' Referral bias (same as Grover 2011): participants who were referred to the consultation-liaison psychiatry team were eligible for the study. It is unknown if all participants with suspected delirium are routinely referred to psychiatry in this hospital</p> <p>Note: Sample size/power calculation not reported.</p>

## Han 2004

Methods	Double-blind, randomised trial of risperidone versus haloperidol in the treatment of delirium	
Participants	Location: Study took place in a single hospital in Korea. Inclusion: All patients presenting with altered mental status who were referred to the consulting psychiatry division were evaluated. Delirium was confirmed with the Confusion Assessment Method and Delirium Rating Scale. Exclusion: any type of dementia or other psychiatric diagnosis, patients already administered an antipsychotic prior to screening for disturbing behavioural problems. Subjects included 24 adult patients (N = 12 haloperidol, mean age 66.5 ± 15.9 years, 7/12 (58%) male, N = 12 risperidone, mean age 65.6 ± 8.3 years, 6/12 (50%) male) from four medical, two intensive care, and two oncology wards, diagnosed with delirium (CAM, DRS)	
Interventions	No placebo group included in this study. Study groups: haloperidol: flexible dose, initial dose of 0.75 mg twice a day versus risperidone: flexible dose, initial dose of 0.5 mg twice a day. Study drug dose was increased depending on the status of delirium during the 7 days of treatment. Delirium was assessed daily. Rescue drugs: None reported	
Outcomes	Outcomes (One psychiatrist, blind to the status of treatment, measured the symptom changes at the same time every day for 7 days): 1. Time to response (Memorial Delirium Assessment Scale (MDAS) score < 13), 2. Response rate (MDAS < 13), 3. Mean drug dose at end of study (day 7). Adverse effects: None included as an outcome. In the results section, it was stated 'None of the 24 subjects who finished the study showed clinically significant side effects'. Method of assessment or which specific side effects examined were not reported	
Notes	Primary investigator supported by the Brain Korea 21 Project of the Ministry of Education and Human Resources Development, Republic of Korea	
Risk of bias		
Bias	Authors' judgement	Support for judgement

**Han 2004** (Continued)

Random sequence generation (selection bias)	Unclear risk	A consulting psychiatrist (not a member of the investigative team) randomly assigned participants without any knowledge of their care. Method of sequence generation not provided
Allocation concealment (selection bias)	Unclear risk	Stated as a double-blind study. However, authors stated it was not possible to obtain identical looking tablets but the 'patients and caretakers did not know the name or effects of their drug'. Likely blinded
Blinding (performance bias and detection bias) All outcomes	Low risk	Stated as a double-blind study. However, authors stated it was not possible to obtain identical looking tablets but the 'patients and caretakers did not know the name or effects of their drug'. Unlikely to have been double-blinded in design. However, a psychiatrist, blind to participant status and treatment, measured symptom change at the same time for a total of 7 days
Incomplete outcome data (attrition bias) All outcomes	High risk	Initially, N = 28 and final sample of N = 24. Two participants in the haloperidol group dropped out: one because of medical deterioration on the second study day, and one because of severe sedation on the third study day. Two participants in the risperidone group dropped out: one because of spousal refusal to participate on the second study day, and one because of a tracheotomy operation on the fourth study day. Attrition not reported in the analysis
Selective reporting (reporting bias)	Unclear risk	Trial protocol not found.
Other bias	Low risk	Sample size calculation not reported.

**Hu 2004**

Methods	Randomised trial comparing olanzapine, haloperidol, and placebo in the treatment of delirium
Participants	Location: Study took place in a single hospital in China. Inclusion: age > 65 years, either male or female, delirium based on DSM-IV, DRS $\geq$ 12, total clinical global impression scale-severity of illness (CGI-SI) > 4. Exclusion: Patients with a severe mental disease, those who had taken any antipsychotic drug, patients with angle-closure glaucoma, paralytic ileus, or material abuse. Subjects

	included 175 hospitalised patients (N = 74 olanzapine, mean age 74 ± 8 years, 45/74 (60.8%) male, N = 72 haloperidol, mean age 74 ± 7 years, 48/72 (66.7%) male, N = 29 placebo, mean age 73 ± 7 years, 18/29 (62.1%) male) with a history of dementia admitted to any of the hospital's wards and diagnosed with delirium (DSM-IV, DRS score ≥ 12 and Clinical Global Impression-Severity of Illness (CGI-SI) score ≥ 4)
Interventions	Study drug: Olanzapine was started at a daily dose of 1.25 to 2.5 mg PO, and increased to a maximum daily dose of 20 mg. Haloperidol was administered in a daily dose range of 2.5 to 10 mg, intramuscularly (starting dose not provided). If CGI-SI score was reduced by ≥ 1, the dose was maintained and study drug was administered for 7 days. All subjects received 'somatic' treatment aimed at the etiological factors of delirium. Delirium was evaluated daily using the DRS and the CGI. Rescue drugs: No other centrally acting drugs were permitted, except in the instance of the development of extrapyramidal symptoms, where a maximum dose of 6 mg of benzhexol was administered
Outcomes	Outcomes (day 7): 1. DRS score, change from baseline to study completion, 2. CGI-SI (Severity) score, change from baseline to study completion, 3. CGI (Global Impression) score, change from baseline to study completion, 4. Dose and time to effect in cases where delirium was successfully treated. Adverse effects: None included as an outcome
Notes	This study was referred to as (Hua 2006) in certain reviews. The original study, cited here, was subsequently translated into English and published under the title 'Olanzapine and haloperidol for senile delirium: a randomised controlled observation'

***Risk of bias***

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No mention of method of randomisation beyond stating participants were randomised in a 5:5:2 ratio to olanzapine, haloperidol, and placebo groups, respectively
Allocation concealment (selection bias)	Unclear risk	No details provided.
Blinding (performance bias and detection bias) All outcomes	High risk	Haloperidol could be given subcutaneously and olanzapine orally. No description of how treatments were concealed. No mention of blinding process. Not likely done
Incomplete outcome data (attrition bias) All outcomes	High risk	No mention of how attrition was factored into statistical analysis (not described as intention-to-treat analysis)
Selective reporting (reporting bias)	Low risk	Trial protocol identified under the first name.

Other bias	Unclear risk	Sample size not reported. Unclear methodology regarding dosing protocol
------------	--------------	---

## Lin 2008

Methods	Randomised trial of haloperidol versus olanzapine in the treatment of delirium
Participants	Location: Study conducted in a single hospital in Taiwan. Inclusion: All participants were recruited from the hospice and palliative care center, had advanced cancer, met the DSM-IV criteria for delirium. Exclusion: past history of psychiatric disorder, coma, could not swallow oral medication, treated with neuroleptic drug within 4 weeks of the study. Subjects included 30 adult palliative and hospice care patients (N = 16 olanzapine, mean age 61.13 ± 16.5 years, 9/16 (56%) male, N = 14 haloperidol, mean age 68 ± 12.14 years, 4/14 (29%) male) diagnosed with delirium (DSM-IV criteria)
Interventions	Study drug: Haloperidol: starting dose of 5 mg PO daily, permitted daily maximum dose 15 mg versus Olanzapine: starting dose of 5 mg PO daily, permitted daily maximum dose 15 mg. Study drug administered for 7 days. Delirium assessed via the Delirium Rating Scale (Chinese version) (DRS-c) at 24 and 48 hours, and one week into treatment. Rescue drugs: If adjunctive therapy required for acute symptoms, midazolam IM was used
Outcomes	Outcomes (day 7): 1. DRS-c at baseline, 24 and 48 hours, and 7 days into treatment, 2. Clinical Global Impression-Severity (CGI-S) at baseline, 24 and 48 hours, and 7 days into treatment. All assessments were conducted by one assessor (research nurse) that was blinded to study assignment. Adverse effects: 1) side effects were observed and recorded on the chart by the clinical team and the assessor of the study without formal instruments
Notes	Trial details/protocol not published in advance.

*Risk of bias*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated as a prospective randomised controlled clinical trial. Likely randomised. Methods of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Insufficient details to assess. Stated that if participant needed an antipsychotic, they were 'separated randomly to an olanzapine group or a haldol group'
Blinding (performance bias and detection bias) All outcomes	Low risk	A single individual, a nurse and counselling psychologist, performed all assessments. The assessor was blinded to subject randomisation



**Lin 2008** (Continued)

Incomplete outcome data (attrition bias) All outcomes	High risk	Total number of participants enrolled and/or lost to follow-up not reported
Selective reporting (reporting bias)	Unclear risk	Outcomes in methods matched those reported in results. Trial protocol not published so unable to confirm all outcomes were reported as planned
Other bias	Unclear risk	Referral bias: A psychiatric specialist determined whether it was necessary for the participant to receive antipsychotic drug treatment based on clinical grounds. If an antipsychotic was deemed needed (criteria for use not provided), the participants were consented and randomised Note: Sample size calculation not reported.

**Maneeton 2013**

Methods	Randomised trial of quetiapine versus haloperidol in the treatment of delirium
Participants	Location: Study took place in a single tertiary care hospital in Thailand. Inclusion: All inpatients presumed to have delirium and needing consultation-liaison services from the psychiatric department were evaluated for inclusion, Delirium confirmed with DSM-IV. Exclusion: substance-induced delirium, known allergy or intolerance to study drugs, pregnancy or breast feeding, already receiving an antipsychotic drug, renal or hepatic failure. Subjects included 52 medically ill adult (aged 18 to 75 years) patients (N = 24 quetiapine, mean age 56.6 ± 12 years, 15/24 (62.5%) male, N = 28 haloperidol, mean age 57 ± 11.9 years, 20/28 (71%) male) diagnosed with delirium (DSM-IV-TR and CAM criteria)
Interventions	Study drugs: Quetiapine: flexible dose ranging from 25 to 100 mg/day versus haloperidol: flexible dose ranging from 0.5 to 2 mg/day. Study drug given at bedtime for 7 days, with additional doses as needed. Drug dose was adjusted based on clinical safety, sleepiness, and calmness, as measured by the Delirium Rating Scale (DRS-R-98). Subject given one dose and another every 2 to 3 hours as needed for agitation, with a daily maximum of four doses. Delirium was assessed daily via the DRS-R-98. All participants were assessed for possible causes of delirium that could be corrected using the mnemonic 'WATCHDEATH'. Environmental manipulations emphasised, such as noise control, light intensity, reassurance, and stimulus modification. Rescue drugs: Other psychotropic drugs, including benzodiazepines, were prohibited
Outcomes	Outcomes (day 7): 1. DRS-R-98 severity score, 2. DRS-R-98 noncognitive and cognitive subscale scores, 3. Delirium response rate (50% reduction of baseline DRS-R-98 score), 4. Delirium remission rate (DRS-R-98 severity score of 12 or less without relapse), 5. Total time of sleep, 6. Clinical Global Impression-Improvement (CGI-I), 7. Modified Simpson-Angus Scale (MSAS). Adverse effects: 1) Participants were assessed for possible adverse events either observed by the investigators, relatives, clinical staff, or self-report.

	Formal tool not used	
Notes	Study funded by the Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand (grant number 077/52)	
<i>Risk of bias</i>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation system. Subjects randomly assigned in a 1:1 manner to one of the two study groups. Randomisation codes were kept in sealed envelopes and opened after the end of the screening process
Allocation concealment (selection bias)	Low risk	Double-blinded study. Study medication, either 25 mg quetiapine or 0.5 mg haloperidol, was fully filled and concealed in identical capsules
Blinding (performance bias and detection bias) All outcomes	Low risk	Double-blinded study. Participants, physicians, staff nurses, investigators, and raters were blinded to treatment assignment
Incomplete outcome data (attrition bias) All outcomes	High risk	Authors reported 32.7% study withdrawal. Stated 13/24 quetiapine- and 22/28 haloperidol-treated participants completed the study. They used intention-to-treat analysis if a participant received at least one dose of the study drug
Selective reporting (reporting bias)	Low risk	Outcomes in methods matched those reported in protocol.
Other bias	Unclear risk	Trial was registered with clinicaltrials.gov (CNT00954603). Referral bias: All inpatients presumed to have delirium and needing consultation-liaison services from the psychiatric department were evaluated for inclusion

Methods	Randomised trial comparing quetiapine versus placebo in the treatment of delirium	
Participants	Location: Study took place in a single hospital in the United Kingdom. Inclusion: DSM-IV criteria for delirium. Exclusion: major pre-existing cognitive deficits (major not defined), alcohol withdrawal, pre-existing psychosis, substance dependence, inability to comply with the constraints of the trial, on medication that interacted with quetiapine. Subjects included 42 patients (N = 21 quetiapine, mean age 84.1 ± 9.45 years, 6/21 (28.6%) male, N = 21 placebo, mean age 84.3 ± 7.16 years, 6/21 (28.6%) male) from medical, surgical, and orthopedic units diagnosed with delirium (DRS-R-98 total score ≥ 15, confirmed by DSM-IV criteria)	
Interventions	Study drugs: Participants received quetiapine or placebo, according to a flexible dosing regimen begun at 25 mg daily, with a dose titration of 25 mg/day to a maximum of 175 mg/day, in divided doses. The dose was increased only if DRS-R-98 and clinical condition showed no improvement and the drug was well tolerated, up to a maximum of 10 days. In addition to the clinical response and tolerability, information from nursing and medical staff was also considered prior to dose changes. If symptoms improved, dose was reduced in a reverse pattern from initial titration. Delirium assessment via DRS-R-98 on study days 1, 2, 3, 4, 7, and 10, with an additional follow-up on day 30. Rescue drugs: Not specified in the methods. However results reported use of lorazepam	
Outcomes	Outcomes (up to day 10): 1. DRS-R-98 score, 2. Mini-Mental Status Examination, 3. Brief Psychiatric Rating Scale, 4. Clinical Global Improvement. Adverse effects: 1. Abnormal Involuntary Movement Scale	
Notes	Investigator-initiated study sponsored by AstraZeneca UK. Funding provided for recruitment of a research assistant and trial medication. AstraZeneca UK also provided the randomisation codes. This study was stopped early	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation codes.
Allocation concealment (selection bias)	Low risk	Computer-generated randomisation codes kept in sealed envelopes in the pharmacy. Set of individual treatment codes kept for emergency out-of-hours use only
Blinding (performance bias and detection bias) All outcomes	Low risk	Double-blinded study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Non-linear, mixed effects models used to estimate differences in recovery trajectories. Reasoning for the use of this statistical method described in a subsequent paper

		published by the authors
Selective reporting (reporting bias)	Low risk	Registered trial.
Other bias	Unclear risk	Sample size calculation reported. The trial was stopped early at the request of the manufacturer due to the FDA's concern on the use of antipsychotic medication in the elderly. The study is, therefore, under-powered. Lorazepam was administered to 4 participants in the the quetiapine group versus none in the placebo group. The quetiapine had faster resolution; unclear if this might have influenced the resolution of symptoms. Investigator-initiated study sponsored by AstraZeneca UK. Funding provided for recruitment of a research assistant and trial medication. AstraZeneca UK also provided the randomisation codes

AIDS=AcquiredImmunodeficiencySyndrome

CAM = Confusion Assessment Method

CGI = Clinical Global Impression

CGI-SI = Clinical Global Impression - Severity Scale index

DRS = Delirium Rating Scale

DRS-c = Delirium Rating Scale (Chinese version)

DRS-R-98 = Delirium Rating Scale Revised 98

DSM = Diagnostic and Statistical Manual of Mental Disorders

IM = Intramuscular injection

MDAS = Memorial Delirium Assessment Scale

NuDESC = Nursing Delirium Screening Scale

PO = *per os* or by mouth

PRN = *pro re nata* or as needed

QTc = QT interval corrected for rate

### Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
<a href="#">Al Qadheeb 2016</a>	Study population was intensive care unit patients.
<a href="#">Atalan 2013</a>	Study population was intensive care unit patients.
<a href="#">Bakri 2015</a>	Study population was intensive care unit patients.

(Continued)

Devlin 2010	Study population was intensive care unit patients.
Girard 2010	Study population was intensive care unit patients.
Hakim 2012	Study population was intensive care unit patients.
Jung 2009	Compared two second generation antipsychotics (risperidone and aripiprazole) with no nonantipsychotic or placebo comparator
Jung 2010	Compared two second generation antipsychotics (risperidone and quetiapine) with no nonantipsychotic or placebo comparator
Kim 2010	Compared two second generation antipsychotics (risperidone and olanzapine) with no nonantipsychotic or placebo comparator
Lee 2005	Compared two second generation antipsychotics (amisulpride and quetiapine) with no nonantipsychotic or placebo comparator
Page 2013	Study population was intensive care unit patients.
Reade 2009	Study population was intensive care unit patients.
Reade 2016	Study population was intensive care unit patients.
Sakong 2010	Compared two second generation antipsychotics (risperidone and aripiprazole) with no nonantipsychotic or placebo comparator
Skrobik 2014	Study population was intensive care unit patients.

## Characteristics of studies awaiting assessment [ordered by study ID]

### Djokic 2008

Methods	Randomised controlled trial to determine the efficiency of risperidone in the treatment of delirium superimposed on dementia
Participants	Study took place in a single hospital in Serbia. N = 120 subjects with mean age of 73.57 years, predominantly female (60.3%), with Alzheimer's disease (60%), dementia in Parkinson's disease (6%), vascular dementia (23%)
Interventions	Participants were randomly assigned to control group (haloperidol 1 to 4 mg/24h) or experimental group (risperidone 0.5 to 2 mg/24h) up to 28 days. Both groups were treated according to the underlying cause of delirium. All participants were assessed with The Memorial Delirium Assessment Scale (MDAS), MMSE, Brief agitation Rating Scale (BARS) and GCI scales daily
Outcomes	1. Change in MDAS scores (day 14, day 28), 2. Change in BARS scores (day 10, day 28), 3. CGI-I scores (day 28), 4. Mortality

**Djokic 2008** (Continued)

Notes	Published in conference abstract form only. Unable to obtain further details from author to establish firm eligibility
-------	--

**Jung Jin 2009**

Methods	Randomised, open prospective study to compare intramuscular olanzapine and intramuscular haloperidol for patients with delirium
Participants	N = 62 hospitalised patients admitted to single hospital in South Korea. Patients were diagnosed as having delirium by two independent psychiatrists using DSM-IV-TR
Interventions	Intramuscular injection olanzapine and intramuscular injection of haloperidol. Details of dose and frequency not provided in the abstract
Outcomes	1. Delirium Rating Scale-revised-98 (DRS-R-98), 2. Clinical Global Impression-Severity (CGI-S), 3. Simpson-Angus Rating Scale, 4. Barnes Akathisia Rating Scale, 5. Abnormal Involuntary Movement Scale
Notes	Numeric results not reported. Published in conference abstract form only. Unable to obtain further details from author to establish firm eligibility

**Lee 2013**

Methods	Randomised trial comparing the efficacy and safety of aripiprazole and haloperidol in the treatment of delirium
Participants	N = 26 patients with delirium (Korean Version of Delirium Rating Scale-revised-98 (KDRS- 98)) 20 participants were analysed at the end.
Interventions	Aripiprazole or haloperidol. No information provided on the dose, titration, formulation, or duration of therapy
Outcomes	1. The Korean Version of Delirium Rating Scale-revised-98 (KDRS- 98) and Korean Version of Drug Induced Extrapyramidal Symptom Scale (DIEPSS-K) were assessed, 2. Blood samples were collected to analyse serum sodium ion concentration, plasma cortisol and prolactin level and pulse oximetry were used for measuring oxygen saturation. Time points of assessment not reported in the abstract
Notes	Numeric results not reported. Published in conference abstract form only. Unable to obtain further details from author to establish firm eligibility

**Nakamura 1997**

Methods	Open label randomised trial of haloperidol and mianserin in the treatment of delirium
Participants	Individuals undergoing neuropsychiatric referrals.
Interventions	Haloperidol: flexible dose of 2 to 6 mg/day per os at bed time. Mianserin: flexible dose of 10 to 60 mg/day per os at bed time

Outcomes	1. Change in delirium severity, as measured by the DRS at baseline and study day 7, 2. Delirium resolution, defined as $\geq 50\%$ reduction in baseline DRS score
Notes	Published in full but unable to obtain further details from author to establish study population, exact number of individuals treated in each group, and delirium inclusion criteria

*BARS= Brief Agitation Rating Scale*

CGI-S = Clinical Global Impression - Severity Scale

CGI-I = Clinical Global Impression - Improvement Scale

DIEPSS-K = Korean Version of Drug Induced Extrapyramidal Symptom Scale

DRS = Delirium Rating Scale

DSM = Diagnostic and Statistical Manual of Mental Disorders

GCI = Clinical Global Impression

KDRS-98 = Korean Version of Delirium Rating Scale-revised-98

MDAS = Memorial Delirium Assessment Scale

MMSE = Mini Mental State Examination

## Characteristics of ongoing studies [ordered by study ID]

### NCT02345902

Trial name or title	Randomised double-blind clinical trial to compare haloperidol and nonpharmacologic treatment versus non-pharmacologic treatment and placebo, in elderly hospitalised patients with hypoactive delirium
Methods	Double-blind RCT of haloperidol versus placebo added to nonpharmacologic treatment for delirium
Participants	Study taking place in a single hospital in Mexico. Participants included hospitalised patients aged 70 years with delirium diagnosis according to the CAM or Delirium Observation Screening Scale (DOSS) and not taking any antipsychotics
Interventions	Haloperidol: 1.25 mg administered orally x 9 days. Placebo: matched placebo tablet, 1.25 mg administered orally x 9 days. Both groups will undergo nonpharmacologic delirium interventions: A. Reorientation (i.e. calendar, clocks, familiar objects), B. Glasses and hearing devices, where needed, C. Avoidance of physical restraints, D. Limitation of excessive personnel shifts or hospital room, E. A tranquil and comfortable environment, especially at night, to avoid interruptions (i.e. dim light, low levels of noise), F. Adequate schedules for medication administration and to take vital signs or medical procedures, G. Sleep hygiene (light in the room and movement during the day), H. Avoidance of dehydration, and I. Avoidance of medications use which are associated with delirium (e.g. psychoactive medications)
Outcomes	1. Change in delirium severity (via Delirium Observation Screening Scale), 2. Use of rescue haloperidol, 3. Duration of delirium, 4. Perceived stress (via Delirium Experience Questionnaire), 5. Incidence of PTSD (Mini International Neuropsychiatry Interview), 6. Cognitive impairment (via Montreal Cognitive Assessment), 7. Cerebral blood flow (via transcranial Doppler), 8. Adverse events (e.g. extrapyramidal symptoms, arrhythmias, QTc prolongation)

**NCT02345902** (Continued)

Starting date	January 2016
Contact information	Dr. Maria Carmen Flores (mcflormir@gmail.com) and Dr. Sara Aguilar-Navarro (sgan30@hotmail.com)
Notes	Study sponsor: Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran. Estimated study completion: October 2018. Trial registration: <a href="https://clinicaltrials.gov/ct2/show/NCT02345902">https://clinicaltrials.gov/ct2/show/NCT02345902</a>

*CAM=ConfusionAssessmentMethod*

DOSS = Delirium Observation Screening Scale

PTSD = Post Traumatic Stress Disorder

QTc = QT interval corrected for rate



## DATA AND ANALYSES

### Comparison 1. Severity of delirium

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Antipsychotic versus no antipsychotic	4	494	Std. Mean Difference (IV, Random, 95% CI)	-1.08 [-2.55, 0.39]
2 Sensitivity analysis (placebo-controlled studies only)	3	464	Std. Mean Difference (IV, Random, 95% CI)	-0.89 [-2.64, 0.86]
3 Sensitivity analysis (trials at low risk of bias)	2	289	Std. Mean Difference (IV, Random, 95% CI)	0.03 [-0.22, 0.27]
4 Typical versus atypical antipsychotic	7	542	Std. Mean Difference (IV, Random, 95% CI)	-0.17 [-0.37, 0.02]

### Comparison 2. Resolution

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Antipsychotic versus no antipsychotic	3	247	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.30, 2.98]
2 Sensitivity analysis (including placebo studies)	2	217	Risk Ratio (M-H, Random, 95% CI)	1.43 [0.58, 3.54]
3 Resolution (atypical versus typical antipsychotic)	5	349	Risk Ratio (M-H, Random, 95% CI)	1.10 [0.79, 1.52]

### Comparison 3. Mortality

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality (antipsychotic versus no antipsychotic)	3	319	Risk Ratio (M-H, Random, 95% CI)	1.29 [0.73, 2.27]
2 Sensitivity analysis (including only placebo studies)	2	289	Risk Ratio (M-H, Random, 95% CI)	1.41 [0.75, 2.66]
3 Mortality (atypical versus typical antipsychotic)	4	342	Risk Ratio (M-H, Random, 95% CI)	1.71 [0.82, 3.53]

## Comparison 4. Adverse Event

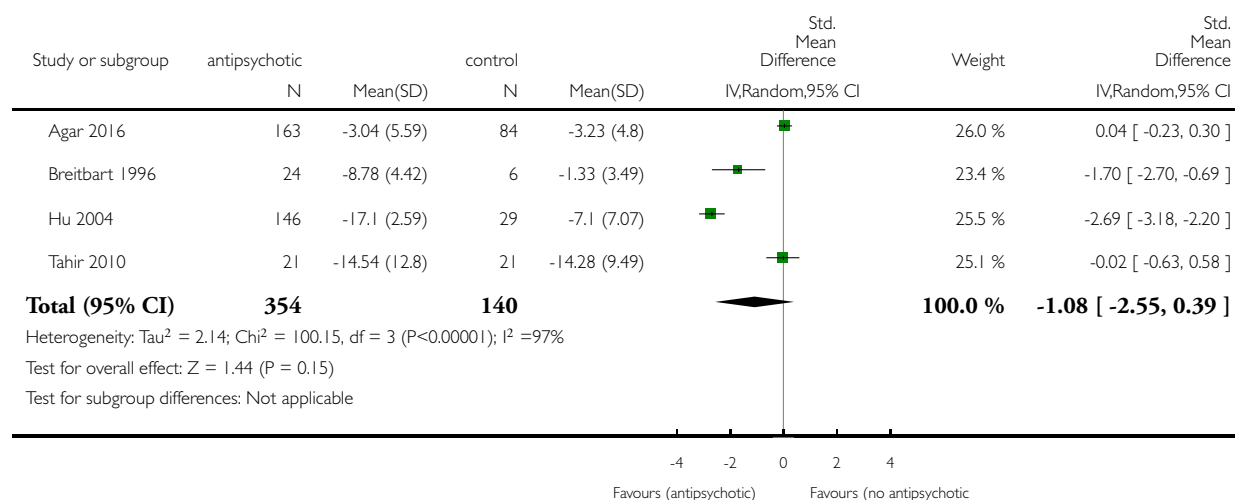
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Antipsychotic versus no antipsychotic (EPS)	3	247	Risk Ratio (M-H, Random, 95% CI)	1.70 [0.04, 65.57]
2 Typical versus atypical antipsychotic (EPS)	2	198	Risk Ratio (M-H, Random, 95% CI)	12.16 [0.55, 269.52]

### Analysis 1.1. Comparison 1 Severity of delirium, Outcome 1 Antipsychotic versus no antipsychotic.

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 1 Severity of delirium

Outcome: 1 Antipsychotic versus no antipsychotic

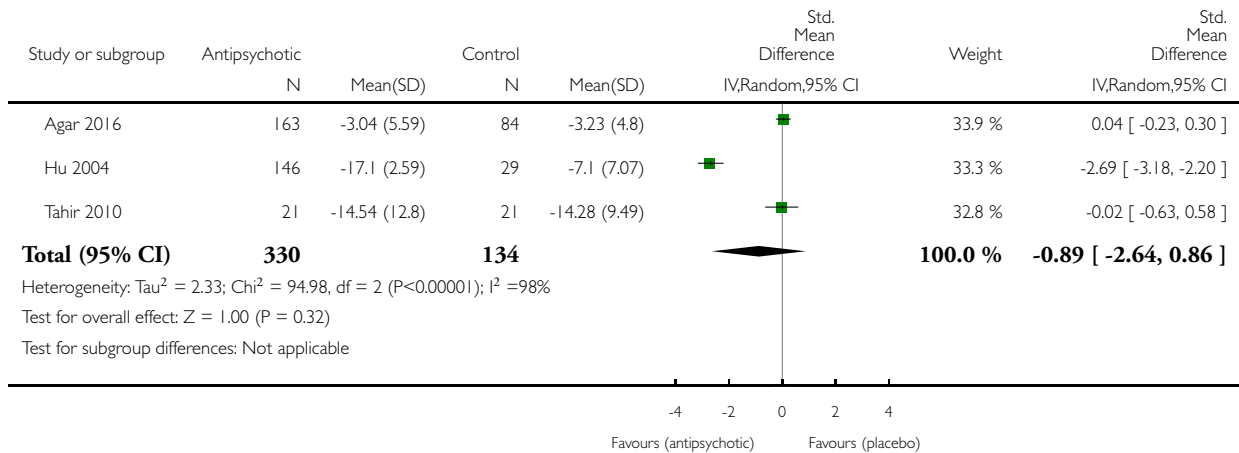


## Analysis 1.2. Comparison 1 Severity of delirium, Outcome 2 Sensitivity analysis (placebo-controlled studies only).

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 1 Severity of delirium

Outcome: 2 Sensitivity analysis (placebo-controlled studies only)

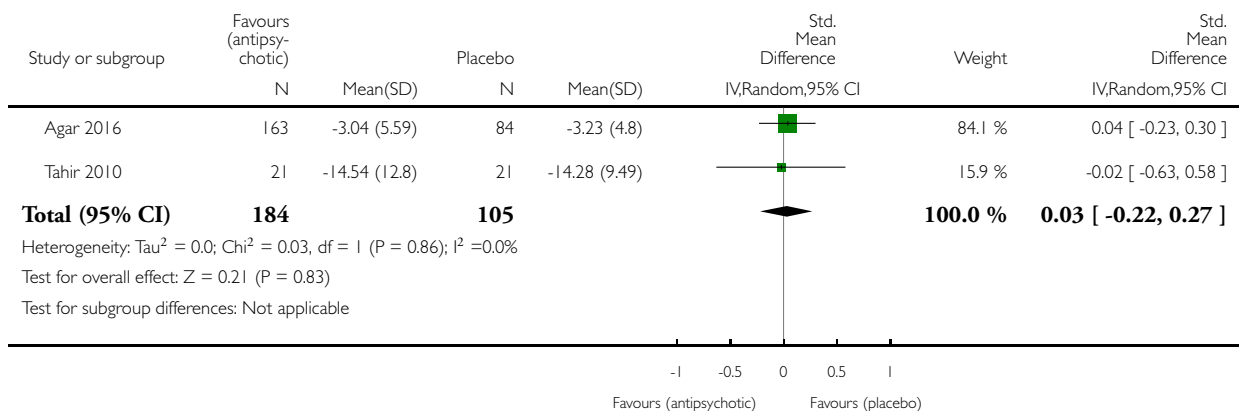


## Analysis 1.3. Comparison 1 Severity of delirium, Outcome 3 Sensitivity analysis (trials at low risk of bias).

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 1 Severity of delirium

Outcome: 3 Sensitivity analysis (trials at low risk of bias)

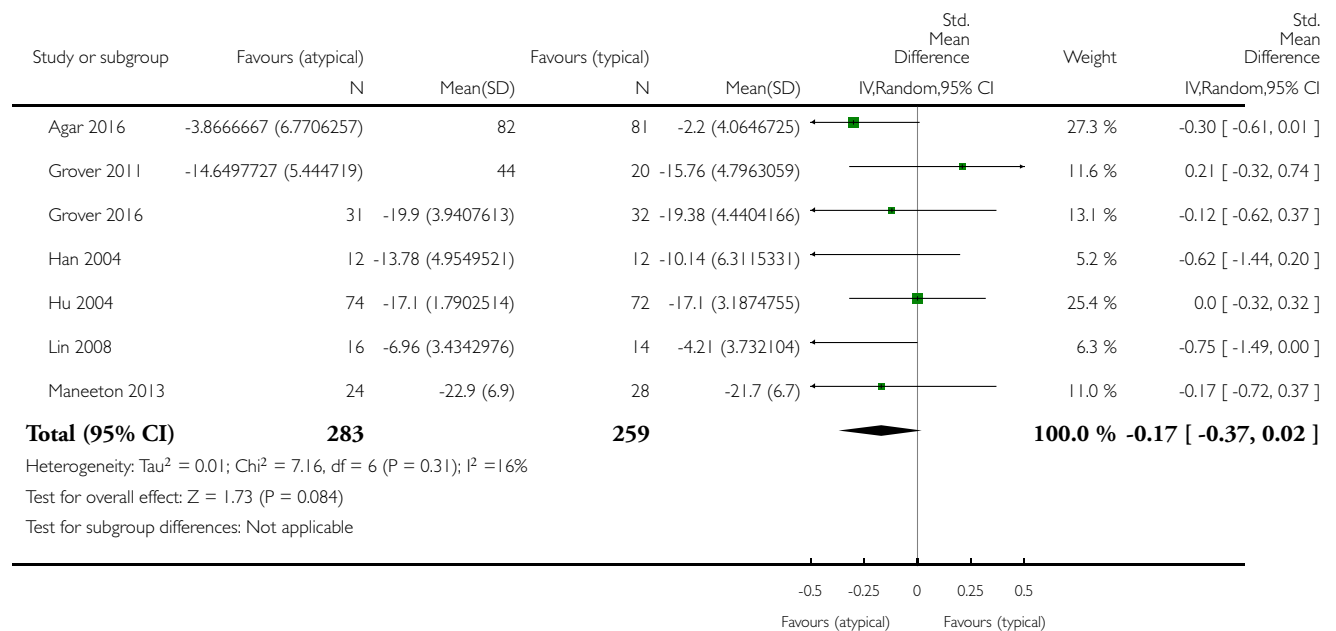


#### Analysis 1.4. Comparison 1 Severity of delirium, Outcome 4 Typical versus atypical antipsychotic.

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 1 Severity of delirium

Outcome: 4 Typical versus atypical antipsychotic

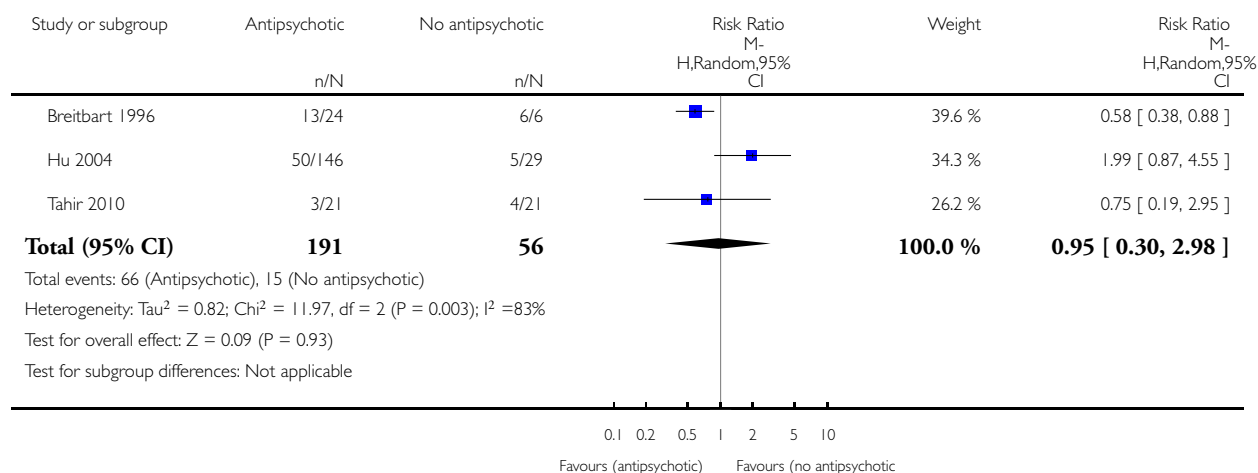


## Analysis 2.1. Comparison 2 Resolution, Outcome 1 Antipsychotic versus no antipsychotic.

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 2 Resolution

Outcome: 1 Antipsychotic versus no antipsychotic

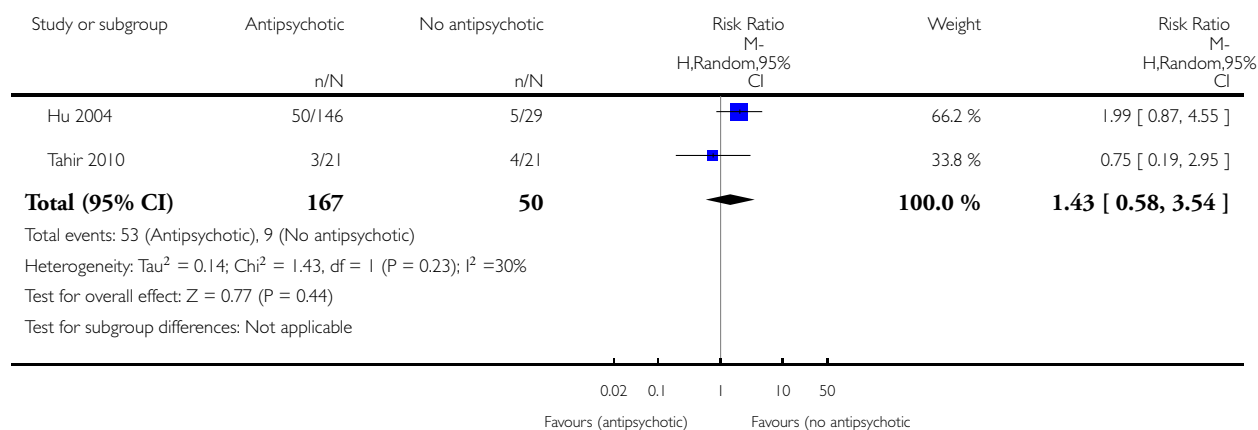


## Analysis 2.2. Comparison 2 Resolution, Outcome 2 Sensitivity analysis (including placebo studies).

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 2 Resolution

Outcome: 2 Sensitivity analysis (including placebo studies)

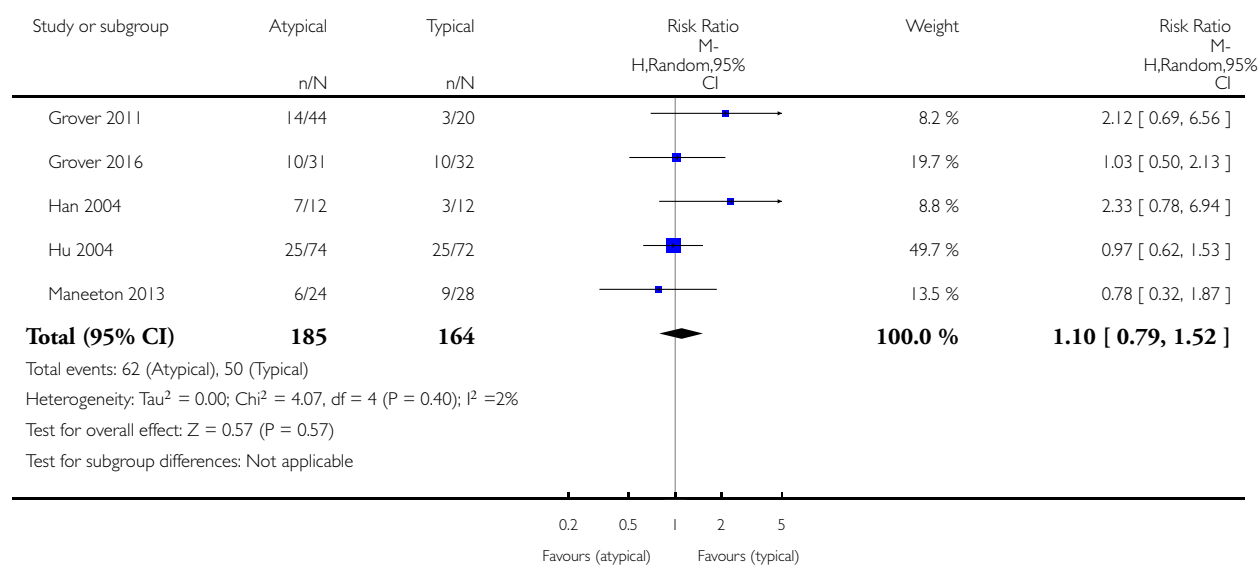


### Analysis 2.3. Comparison 2 Resolution, Outcome 3 Resolution (atypical versus typical antipsychotic).

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 2 Resolution

Outcome: 3 Resolution (atypical versus typical antipsychotic)

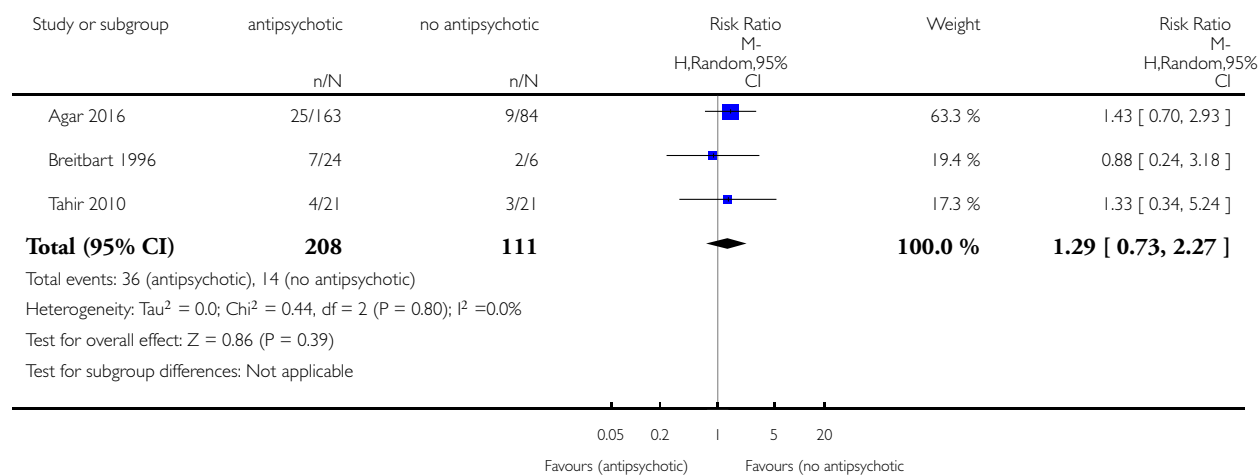


### Analysis 3.1. Comparison 3 Mortality, Outcome 1 Mortality (antipsychotic versus no antipsychotic).

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 3 Mortality

Outcome: 1 Mortality (antipsychotic versus no antipsychotic)

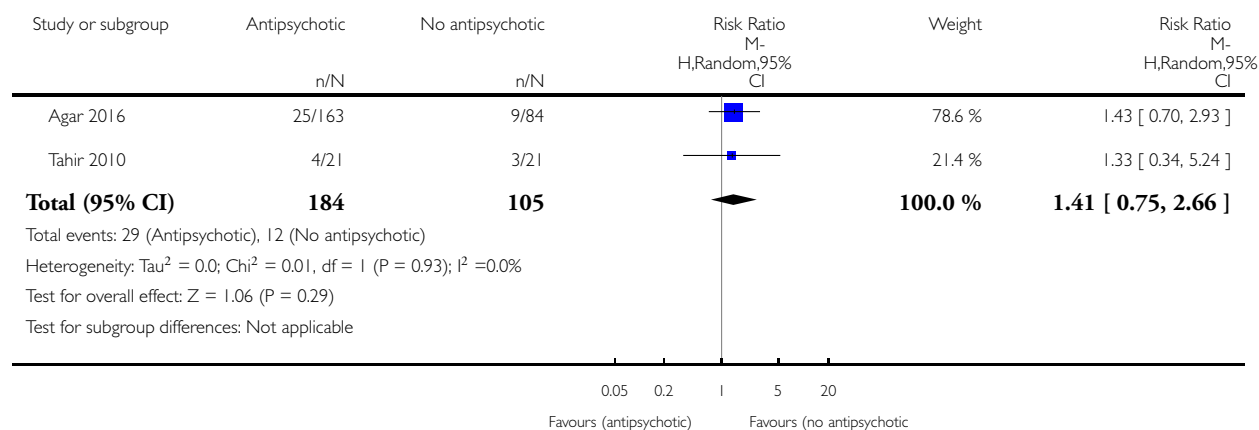


### Analysis 3.2. Comparison 3 Mortality, Outcome 2 Sensitivity analysis (including only placebo studies).

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 3 Mortality

Outcome: 2 Sensitivity analysis (including only placebo studies)

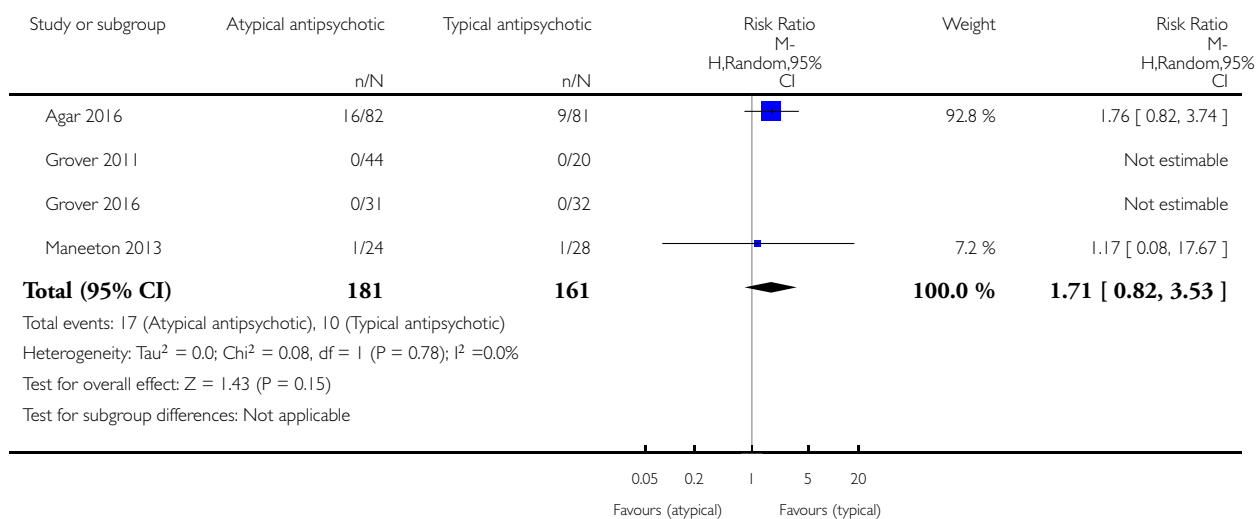


### Analysis 3.3. Comparison 3 Mortality, Outcome 3 Mortality (atypical versus typical antipsychotic).

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 3 Mortality

Outcome: 3 Mortality (atypical versus typical antipsychotic)



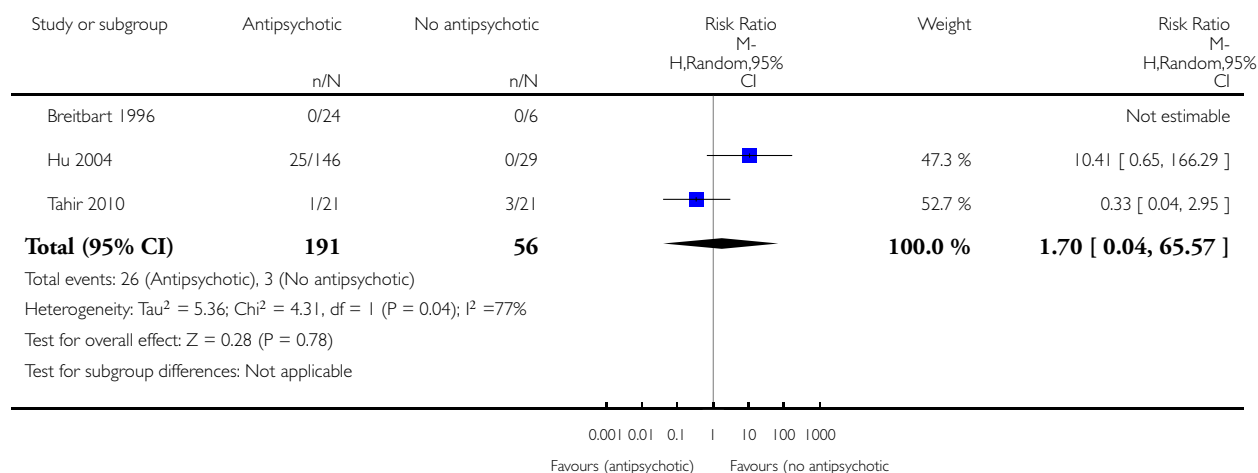


#### Analysis 4.1. Comparison 4 Adverse Event, Outcome 1 Antipsychotic versus no antipsychotic (EPS).

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 4 Adverse Event

Outcome: 1 Antipsychotic versus no antipsychotic (EPS)

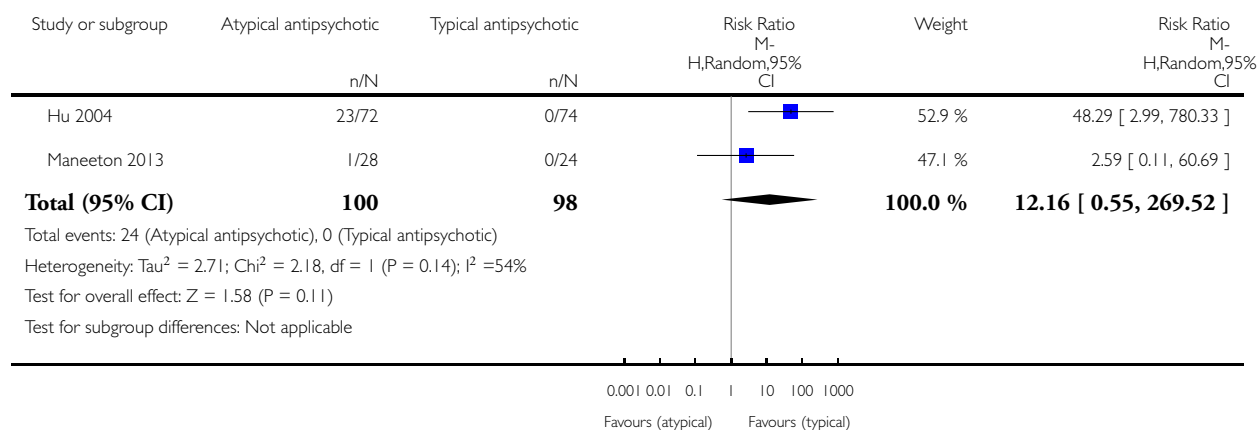


#### Analysis 4.2. Comparison 4 Adverse Event, Outcome 2 Typical versus atypical antipsychotic (EPS).

Review: Antipsychotics for treatment of delirium in hospitalised non-ICU patients

Comparison: 4 Adverse Event

Outcome: 2 Typical versus atypical antipsychotic (EPS)



## APPENDICES

### Appendix I. MEDLINE Search Strategy

Database: Ovid MEDLINE(R) 1946 to July 20, 2017 with Daily Update

Search Strategy:

- 
- 1 Antipsychotic drugs/ or (antipsychotic\* or neuroleptic\* or (major adj2 (tranquilizer\* or tranquiliser\*))).mp.
  - 2 (aceperone or acetabutone or acetobutone or "r 3248" or r3248).mp.
  - 3 Acepromazine/ or (acepromazine or acetopromazine or vetranquil or acetylpromazine or acepromazine or calmivet or acetazine or notensil or plegicil or promace or soprintin or anatan or anergan or atravet or "cb 1522" or cb1522 or plegicin or plegicyl or sedalin or soprintin).mp.
  - 4 (aceprometazine or acepromethazine or acetylpromethazine).mp.
  - 5 (acetophenazine or acephenazine or "nsc 70600" or nsc70600 or "sch 6673" or sch6673 or tindal).mp.
  - 6 (adoprazine or adoprazin or "slv 313" or slv313).mp.
  - 7 (alimemazin or alimemasine or alimemazin\* or alimezine or "bayer 1219" or electrotrimeprazine or methylpromazine or palpex or "rp 6549" or rp6549 or trimeprazine or trimeprezine or varialgil or nedeltran or panectyl or repeltin or temaryl or temaryl or teralen or teralene or theralen or theralene or valergan or vallergeran).mp.
  - 8 ("bms 181100" or bms181100 or "bmy 14802" or "bmy 14802 1" or "bmy 14802-1" or bmy14802 or "bmy14802 1" or "bmy14802-1" or bmy148021).mp.
  - 9 ("s 16924" or s16924).mp.
  - 10 (amitriptyline or ((amitriptyline adj2 perphenazine) or "anxipress-d" or "duo-vil 2-10" or "duo-vil 2-25" or "duo-vil 4-10" or etrafon or etraphon or longopax or mutabon or mutanxion or mutaspline or "neuragon-a" or "neuragon-b" or peritriptyl or polybon or triavil or triptafen)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
  - 11 (aplindore or "dab 452" or dab452 or palindore or "way dab 452" or "way dab452").mp.
  - 12 ((atypical adj2 (antipsychotic\* or neuroleptic\*)) or abaperidone or "fi 8602" or fi8602 or alentamol or alentemol or "u 66444b" or "u 68552b" or "u 68553b" or u66444b or u68552b or u68553b or aminosultopride or amisulpiride or amisulpridum or "dan 2163" or dan2163 or sertol or socian or solian or amperozide or "fg 5606" or fg5606 or aripiprazole or abilify or abilitat or "opc 14597" or opc14597 or asenapine or "org 5222" or org5222 or saphris or sycrest or batelapine or "cgs 13429" or cgs13429 or belaperidone or balaperidone or "lu 111995" or lu111995 or bifeprunox or "du 127090" or du127090 or emonapride or emirace or nemonapride or "ym 09151" or "ym 09151 02" or "ym 09151 2" or "ym 09151-02" or "ym 09151-2" or ym09151 or "ym09151 02" or "ym09151 2" or "ym09151-02" or "ym09151-2" or ym0915102 or ym091512 or elopiprazole or flumezapine or "ly 120363" or ly120363 or fluoxetine or symbyax or fluperlapine or "nb 106689" or nb106689 or iloperidone or fanapt or fanaptum or "hp 873" or hp873 or "ilo 522" or ilo522 or zomaril or lurasidone or latuda or "mk 3756" or mk3756 or "sm 13496" or sm13496 or "smp 13496" or smp13496 or melperone or bunil or buronil or eunerpan or "fg 5111" or fg5111 or flubuperone or melperon or methylperone or metylperone or metylperonum or "sdz 208 912" or "sdz 208-912" or "sdz 208912" or "sdz 912" or "sdz hdc 912" or "sdz hdc912" or "sdz208 912" or "sdz208-912" or sdz208912 or sdz912 or "sdz 208 911" or "sdz 208-911" or "sdz 208911" or "sdz 911" or "sdz hac 911" or "sdz hac911" or "sdz208 911" or "sdz208-911" or sdz208911 or sdz911 or "fg 5803" or fg5803 or norclozapine or demethylclozapine or desmethylclozapine or ocapridone or "r 79598" or r79598 or olanzapine or anzatric or "dopin tab" or "jolyon md" or lanopin or lanzac or "ly 170053" or ly170053 or meltolan or midax or olace or oladay or olan or olandus or olanex or olansek or olapin or olazax or oleanz or olexar or oltal or olzap or onza or "ozapin md" or psychozap or relprev or zalasta or zelta or zydis or zypadhera or zyprex or zyprexa or zyprexav or paliperidone or invega or "paliperidone palmitate" or "r 76477" or r76477 or "ro 76477" or "ro 92670" or ro76477 or ro92670 or xeplion or panamesine or "emd 57445" or emd57445 or pentiapipe or "cgs 10746" or cgs10746 or "cgs 10746b" or cgs10746b or perlapine or "aw 14'2333" or "aw 142333" or aw142333 or perlapipe or perospirone or lullan or "sm 9018"

or sm9018 or pridopidine or "acr 16" or acr16 or "asp 2314" or asp2314 or "fr 310826" or fr310826 or huntexil or quetiapine or "ici 204636" or "ici 204646" or ici204636 or ici204646 or seroquel or socalm or tienapine or remoxipride or "a 33547" or a33547 or "fla 731" or fla731 or roxiam or rilapine or sertindole or "lu 23174" or lu23174 or "s 1991" or s1991 or serdolect or serlect or sulpiride or abilit or aiglonyl or arminol or dobren or dogmatil or dogmatyl or dolmatil or eglonyl or equilid or "fk 880" or fk880 or isnamide or levobren or levopraid or levosulpiride or meresa or miradol or neogama or sulfiride or sulpivert or sulpyride or synedil or vipral or sultopride or barnetil or barnotil or "ms 5024" or ms5024 or sulfopride or tenilapine or tiospirone or "bmy 13859" or bmy13859 or "mj 13859" or "mj 13859 1" or "mj 13859-1" or mj13859 or "mj13859 1" or "mj13859-1" or mj138591 or tiaspirone or volinanserine or "m 100907" or m100907 or "mdl 100151" or "mdl 100907" or mdl100151 or mdl100907 or ziprasidone or "cp 88059" or "cp 88059 01" or "cp 88059 27" or "cp 88059-01" or "cp 88059-27" or "cp 8805901" or "cp 8805927" or cp88059 or "cp88059 01" or "cp88059 27" or "cp88059-01" or "cp88059-27" or cp8805901 or cp8805927 or geodon or zeldox or zeldrox or zipsydon or zotepine or lodopin or nipolept).mp.

13 Azaperone/ or (azaperone or "r-1929" or r1929 or sedaperone or stresnil).mp.

14 Benperidol/ or (benperidol or anquil or benperidone or benzoperidol or benzperidol or benperidolneuraxpharm or "cb 8089" or cb8089 or frenactyl or frenactil or glianimon or "mcn jr 4584" or "mcn jr4584" or phenactil or "r 4584" or r4584).mp.

15 (berupipam or "nnc 22 0010" or "nnc22 0010").mp.

16 (bitopertin or paliflutine or "r 1678" or r1678 or "rg 1678" or rg1678 or "ro 4917838" or ro4917838).mp.

17 (blonanserine or "ad 5423" or ad5423 or lonasen).mp.

18 (brexpiprazole or "opc 34712" or opc34712).mp.

19 (brofexine or dimetabrone or "fi 6820" or fi6820).mp.

20 (bromospiperone or bromospiroperidol).mp.

21 (bromperidol or impromen or "r 11,333" or "r 11333" or "r11,333" or r11333 or tesoprel or "impromen decanoate" or "r 46,541" or "r 46541" or "r46,541" or r46541).mp.

22 Butaclamol/ or Dibenzocycloheptenes/ or ("ay 23,028" or "ay 23028" or "ay23,028" or "ay-23028" or ay23028 or butaclamol).mp.

23 (butaperazine or "ahr 3000" or "bayer 1362" or butaperazinum or butyrylperazin or butyrylperazine or megalactil or randolectil or randolectyl or repoise or "riker 595" or tyrylen).mp.

24 (carfenazine or carfenazinum or carphenazine or "nsc 71755" or nsc71755 or procethazine or proketazine or "wy 2445" or wy2445).mp.

25 (cariprazine or "mp 214" or mp214 or "rgh 188" or rgh188).mp.

26 (carpipramine or carbadipimidine or defecton or defekton or prazinil or "pz 1511" or pz1511 or "rp 21679" or rp21679).mp.

27 (carvotroline or "wy 47791" or wy47791).mp.

28 centbutindole.mp.

29 (chlorothiazide or "diupres-250" or "diupres-500").mp.

30 (chlorphenethazine or chlorfenethazine or elroquil or marophen).mp.

31 (chlorproethazine or neurilege or "rp 4909" or rp4909).mp.

32 chlorpromazine/ or (chlorpromazine or "2601 a" or "4560 r p" or aminasin or aminasine or aminazin or aminazine or ampliactil or ampicil or ancholactil or aspersinal or bellacina or cepezet or chlormazine or "chlor pz" or chloractil or chlorazine or chlorbromasin or chlorderazine or chlorderazin or chlormazine or chlorpromanyl or chlorpromazin or chlorpromed or clonazine or clordelazin or clorpromaz or clorpromazine or clozine or contomin or duncan or elmarin or esmino or fenactil or hibanil or hibernal or hibernal or "hl 3746" or "hl 5746" or klorproman or klorpromazin or klorpromex or laractyl or largactil or largactyl or matcine or megaphen or megatil or "ml 5746" or neomazine or neurazine or novomazine or phenathyl or plegomazin or plegomazine or proma or promacid or promactil or promapar or promazil or promexin or propaphen or propaphenin or prozil or prozin or psychozine or psynor or "rp 4560" or sanopron or "skf 2601 a" or solidon or sonazine or taroctil or taroctyl or "thor prom" or thorazene or thorazine or torazina or "vegetamin a" or "vegetamin b" or winsumin or wintamine or wintermin or zuledin or "thora-dex" or opromazine or secotil).mp.

33 Chlorprothixene/ or (chlorprothixene or chloprothixene or "chlor prothixene" or chloroprothixene or chlorprothixen or chlorprothixenechloride or chlorprotixen or chlorprotixene or chlothixen or "n 714" or "n 7714" or "ro 4 0403" or "ro 40403" or taractan or tarasan or traquilan or troxen or truxal or truxaleta or truxaletten).mp.

34 chlorprothixene/ or (chlorprothixene or chloprothixene or "chlor prothixene" or chloroprothixene or chlorprothixen or chlorprothixenechloride or chlorprotixen or chlorprotixene or chlothixen or "n 714" or "n 7714" or "ro 4 0403" or "ro 40403" or taractan or tarasan or traquilan or troxen or truxal or truxaleta or truxaletten).mp.

35 (cinuperone or "hr 375" or hr375).mp.

36 (docapramine or "y 4153" or y4153).mp.

37 ("cloflumide mesylate" or "vufb 15496" or vufb15496).mp.

38 (clofluperol or seperidol).mp.

39 Clopenthixol/ or THIOXANTHENES/ or TRANQUILIZING AGENTS/ or (clopenthixol or “ay 62021” or ay62021 or chlorpenthixol or chlorperphenthixene or chlorperphenthixene or ciaryl or cisordinol or clopenthixol or cloxipol or “n 746” or n746 or “nsc 64087” or nsc64087 or sordinol or zuclopenthixol).mp.

40 (clopimozide or “r 29,764” or “r 29764” or “r29,764” or r29764).mp.

41 (clopipazan or “skf 69634” or skf69634).mp.

42 (clopipramine or cremin or mosapramine or “y 516” or y516).mp.

43 (clotiapine or clothiapin or clothiapine or entumin or entumine or etumine or “hf 2159” or hf2159).mp.

44 (“cp 903397” or cp903397).mp.

45 Clozapine/ or Dibenzazepines/ or Piperazines/ or (alemoxan or azaleptin or clopine or clopsine or clozapin\* or clozaril or denzapine or dorval o rdopazine or elcrit or fazaclo or “hf 1854” or hf1854 or lapenax or leponex or lozapin\* or sizopin or versacloz or “wander compound” or zapen or zaponex).mp.

46 (cyamemazine or cianatil or cyamepromazine or “fi 6229” or fi6229 or kyamepromazin or “rp 7204” or rp7204 or tercián).mp.

47 ((dextroamphetamine adj2 sulfate adj2 prochlorperazine) or “eskatrol spansule”).mp.)

48 ((dexamphetamine or dexserpine or dextroamphetamine) adj2 reserpine).mp.

49 ((diethylstilbestrol adj2 methyltestosterone) or tylandril).mp.

50 (dimetotiazine or banistyl or dimethiotazine or dimethiothazine or dimethothiazine or dimethotiazine ro dimetiotazine or fonazine or “il 6302”).mp.

51 ((dimevamide adj2 phenobarbital) or “neuro-centrine tablet\*”).mp.

52 (dixyrazine or dixirazine or dixyrazin or dyxirazine or esocalm or esucos or metronal or roscal or “ucb 3412” or ucb3412).mp.

53 (dolasetron or anemet or anzemet or “mdl 73147” or “mdl 73147ef” or mdl73147 or mdl73147ef or zamanon).mp.

54 Droperidol/ or (droperidol or dehidrobenzoperidol or dehydrobenzoperidol or dehydrobenzoperiol or dehydrobenzperidol or dehydrobenzperidolum or dridol or droleptan or droperol or halkan or inaprine or inapsin or inapsine or “mcn jr 4749” or “mcn r 4749” or oridol or “r 4749” or sintodian or troperidol or xomolix or innovan or innovar or inoval or inovar or talamonal or thalamonal or disifelit).mp.

55 (duoperone or “ahr 6646” or ahr6646).mp.

56 ((ephedrine adj2 sulfate) or renir).mp.

57 ((ethinylestradiol adj2 reserpine) or estrosed or sergynol).mp. (

58 (etymemazine or diquel or ethotrimprazine or ethylisobutrazine or ethymemazine or nuital or “rp 6484” or rp6484 or sergetyl).mp.

59 Etazolate/ or Pyridines/ or (etazolate or sq20009 or “sq-20009” or “sq 20009”).mp.

60 (farampator or “cx 691” or cx691 or “org 24448” or org24448).mp.

61 (fluanisone or “anti pica” or antipica or fluanison\* or fluanizone or fluoanisone or haloanison or haloanisone or “md 2028” or md2028 or “r 2028” or “r 2167” or r2028 or r2167 or sedalande or sedalanide or solusediv).mp.

62 Flupenthixol/ or (flupentixol or flupenthixol\* or emergil or fluaxnol or fluxanxol or “lc 44” or lc44 or “n 7009” or n7009 or siplaril or siplarol or depixol or depot or “lu 5 110” or “lu 5110” or viscoleo).mp.

63 Fluphenazine/ or (fluphenazin\* or anatensil or anatensol or antasol or cenilene or dapotum or elinol or flufenan or flufenazine or flumezin or fluorfenazine or fluphenacin or “fluzine-p” or ftorphenazine or “luogen depot” or lyogen or lyorodin or moditen or moditin or omca or pacinol or permitil or phthorphenazine or potensone or prolixan or proluxene or prolixin\* or “s 94” or sevinol or sevinol or squaline or squalon\* or siquoline or “sq 4918” or sq4918 or tensofin or trancin or valamina or vespazin\* or “dapatum d25” or dapotum or decafen or flucan or fludecasine or fludecate or lyogen or mirenil or modecate or phlufdek or sydepres or flunanthane).mp.

64 Fluspirilene/ or (fluspirilene or fluspi or fluspirilen or imap or “mcn jr 6218” or “mcn jr6218” or “r 6218” or r6218 or redeptin or spirodiflamine or kivat).mp.

65 (flutroline or “cp 36,584” or “cp 36584” or “cp36,584” or cp36584).mp.

66 ((endorphin adj2 deenkephalin) or “beta endorphin[6-17]” or “beta lipotropin[66-77]” or “org 5878” or org5878).mp.

67 (gevetroline or “wy 47384” or wy47384).mp.

68 penite.mp.

69 Haloperidol/ or (haloperidol or alased or aloperidin\* or avant or binison or brotopon or celenase or cereen or cerenace or cizoren or depidol or dores or dozic or duraperidol or “einalon s” or fortunán or govotil or haldol or halidol or “halo-p” or halojust or halomed or haloneural or haloper or haloperil or haloperin or haloperitol or halopidol or halopol or halosten or haricon or “haridol-d” or keselan or linton or “lodomer-2” or “mcn jr 1625” or “mcn jr1625” or mixidol or novoperidol or “nsc 170973” or nsc170973 or peluces or perida or peridol or peridor or “r 1625” or r1625 or selezyme or seranace or serenace or serenase or serenelfi or siegoperidol or sigaperidol or trancodol or pericate or “r 13,672” or “r 13672” or senorm).mp.

70 (hexamethonium or reserthonium).mp.

71 (dralserp or (hydralazine adj2 reserpine) or "serpasil-apresoline" or "hydropresor dichlotride s" or "h.r.-50" or "hydro-reserp" or hydrochlorothiazide or hydroserpine or "medeserpine co" or "serpasil-esidrix").mp.

72 ((hydrochlorothiazide adj2 reserpine adj2 secbutabarbital) or butiserpazide).mp.

73 ((hydroflumethiazide adj4 reserpine) or rautrax).mp.

74 ((hydroflumethiazide adj2 reserpine) or salutensin\*).mp.

75 (isofloxythepin or "vufb 10662").mp.

76 (isomolpan or "cgs 15855" or "cgs 15855 a" or "cgs 15855a" or cgs15855 or cgs15855a).mp.

77 ((isopropamide adj4 prochlorperazine) or "combid spansule").mp.

78 (lenperone or "ahr 2277" or ahr2277 or elanone).mp.

79 (levomepromazine or "apo-methoprazine" or "bayer 1213" or "cl 36467" or "cl 39743" or cl36467 or cl39743 or hirnamin or mepromazine or levium or promazine or levomeprazine or levopromazin\* or levoprome or levozin or mepromazine or methotrimeprazine or methozane or milezin or minozinan or neozine or neuractil or neurocil or nirvan or nozinan or "rp 7044" or rp7044 or sinogan or "sk and f 5116" or "skf 5116" or skf5116 or tiscerin or tiscerin or veractil).mp.

80 lithium/ or lithium.mpp.

81 Loxapine/ or (loxapine or adasuve or "alxz 004" or alxz004 or "az 004" or az004 or "cl 62,362" or "cl 62362" or "cl62,362" or cl62362 or "cl 71563" or "cl-71563" or cl71563 or loxapinsuccinate or cloxazepin\* or loxapane or loxapin\* or loxitane or oxilapine or "sum 3170" or sum3170 or daxolin or desconex or loxapac).mp.

82 maroxepine.mpp.

83 (mazapertine or "rwj 37796" or rwj37796).mp.

84 (mepiprazole or "emd 16923" or emd16923 or psigodal or prozine or meprobamate).mp.

85 Mesoridazine/ or Phenothiazines/ or Tranquilizing Agents/ or (mesoridazin\* or esoridazine or lidanar or lidanil or mesorin or "nc 123" or (thioridazine adj2 sulfoxide) or "tps 23" or serentil).mp.

86 ((methamphetamine adj2 reserpine) or "du-oria").mp.

87 Methiothepin/ or Dibenzothiepins/ or Piperazines/ or (methiothepin\* or metitepine).mp.

88 (methopromazine or methoxympromazine or metopromazine or "diutensen-r").mp.

89 Methotrimeprazine/ or (levopromazine or tizercine or methotrimeprazine or levomepromazine or levomeprazin or tiscerin or tizertsin).mp.

90 (metofenazate or frenolon or metaphenazine or methophenazine or metophenazine or phrenolon).mp.

91 Molindone/ or indoles/ or (molindon\* or "en 1733a" or en1733a or lidone or moban or molindor).mp.

92 (moperone or luvatren or luvatrena or "methyl peridol" or methylperidol\* or moperon or "r 1658").mp.

93 ("y 20024" or y20024).mp.

94 ("alx 5407" or alx5407 or NFPS).mp.

95 ("sb 277011" or "sb 277011a" or sb277011 or sb277011a).mp.

96 (neboglamine or "cr 2249" or cr2249 or "xy 2401" or xy2401).mp.

97 ((nicotinic adj4 pentetrazole adj4 reserpine) or (nicozol adj2 reserpine)).mp.

98 noctran.mpp.

99 (norchlorpromazine or demethylchlorpromazine or demonomethylchlorpromazine or desmethylchlorpromazine or desmonomethylchlorpromazine or monodesmethylchlorpromazine).mp.

100 Ondansetron/ or Imidazoles/ or (ondansetron or gr38032f or "gr 38032f" or "sn 307" or sn307 or "gr-38032f" or "sn-307" or zofran).mp.

101 (oxiperomide or "r 4714" or r4714).mp.

102 (oxypertin\* or "cl 77328" or cl77328 or equipertine or forit or opertil or oxipertin or oxypertin or "win 18501 2" or "win 18501-2" or "win 185012" or "win18501 2" or "win18501-2" or win185012).mp.

103 (oxyprothepine or oxyprothepin).mp.

104 (pecazine or lacumin or mepasin or mepazine or nothiazine or "p 391" or pacatal or pacatol or pactal or papital or paxital or pecazine or "w 1224").mp.

105 Penfluridol/ or (penfluridol or "mcn jr 16,341" or "mcn jr 16341" or micefal or "r 16,341" or "r 16341" or semap or "r 16341" or "r-16341" or r16341).mp.

106 Perazine/ or (perazine or taxilan).mp.

107 (pentaerythrityl or pentaserpine or respet or pentraline).mp.

108 ("nambu-serpine" or (pentobarbital adj2 reserpine)).mp.

109 (perazine or "p 725" or pernazine or taxilan).mp.

- 110 (periciazine or aolept or neulactil or neuleptil\* or periciazinum or pericyazine or properciazine or propericiazin or propericiazine or “rp 8909” or “skf 20716”).mp.
- 111 (perimetazine or “1317 an” or “an 1317” or an1317 or leptyl or perimethazine).mp.
- 112 Perphenazine/ or (perphenazine or chlorperphenazine or chlorpiprazine or chlorpiprozone or decentan or etaperazine or ethaperazine or “f-mon” or fentazin or leptopsique or peratsin or perfenazine or perferazine or pernamed or perphenan or perphenazin\* or “perzine-p” or porazine or “sch 3940” or thilatazin or tranquisan or trifalon or trilafan or trifalon or trilifan or triliphan or triomin).mp.
- 113 (“pf 217830” or pf217830 or “pf 2400013” or pf2400013 or “pf 3463275” or pf3463275).mp.
- 114 ((phenobarbital adj2 reserpine) or “solfo-serpine” or bromoserpin or “theo-serp” or “theobarb-r” or theoserpin or besertal or “neo-slowten”).mp.
- 115 (picobenzide or dosetil or “m 14012 4” or “ma 14012” or picobenzamide).mp.
- 116 piflutixol.mp.
- 117 (pimavanserin or “acp 103” or acp103).mp.
- 118 (pimethixene or “bp 400” or “bp 400 e” or “bp 400e” or bp400 or bp400e or muricalm or pimetixin).mp.
- 119 Pimozide/ or (pimozide or antalon or “mcn jr 6238” or opiran or orap or pimocide or pimoride or pinozide or pizide or “r 6238” or r6238).mp.
- 120 (pipamperone or dipeperon or dipiperon or “dl piperonyl” or floropipamide or “piperonyl of pripamperone of r 3345” or r3345).mp.
- 121 (piperacetazine or “pc 1421 or pc1421” or quide).mp.
- 122 (pipotiazine or “9366 rp” or piportil or pipothiazine or “rp 19366” or rp19366 or “il 19552” or il19552 or “rp 19552” or rp19552 or rp 19551).mp.
- 123 (pirenperone or “r 47,465” or “r 47465” or “r 50656” or “r47,465” or r47465 or r50656 or “renese r” or “renese-r”).mp.
- 124 (“pomaglumetad methionil” or “ly 2140023” or ly2140023).mp.
- 125 Prochlorperazine/ or (compazine or prochlorperazine or “6140 rp” or antinaus or “bayer a 173” or “bayer 173” or capazine or chlormeprazine or chlorpeazine or chlorperazine or compro or dicopal or emelent or klometil or kronocin or meterazine or metherrazine or nautisol or nipodal or normalmin or pasotomin or prochlor or prochlorpemazine or prochlorperacine or prochlorperzine or prochlorpromazine or proclorperazine or procot or “rp 6140 ir rp6140” or “sk and f 4657” or “skf 4657” or skf4657 or temetil or temetil or buccastem or dhaperazine or emeteral or emetiral or nibromin or proclozine or procomp or stemetil or stemzine).mp.
- 126 (profenamine or dibutil or ethopropazine or etopropazine or isothazine or isothiazine or lysivane or parcidol or pardisol or parfezin\* or parkisol or parphezin or parsidol or parsitan or phenopropazine or “profenamine hydrochloride” or prophenamine or rochipel or rodipal or “rp 3356” or “sc 2538”).mp.
- 127 Promazine/ or (promazine or alofen or alophen or ampazine or amprazim or centractyl or delazin or esparin or lete or liranol or “neo hibernex” or neuroplegil or piarine or prazine or “pro tan” or promantine or promanyl or promilene or promwill or protactil or protactyl or romthiazine or romtiazin or “rp 3276” or sediston or sinophenin\* or sparine or tomil or varophen or verophen or “wy 1094”).mp.
- 128 ((propantheline adj4 thiopropazate) or “pro-banthine”).mp.
- 129 (propiomazine or “cb 1678” or cb1678 or largon or propionylpromethazine or propiomazine or propromazine or dorevane or indorm or phenoctyl or propavan or “wy 1359”).mp.
- 130 (propionylpromazine or combelen or dipropiomazine or propiopromazine or tranvet).mp.
- 131 (prothipendyl or “ay 5603” or ay5603 or azacon or “d 206” or d206 or dominal or inalforte or largophren or “lg 206” or lg206 or phrenotropin or prothipendil or protipendil or protipendyl or timovan or tolnate or tumovan).mp.
- 132 (protoveratrine or “veralba r” or verapene or “protalba-r” or pyrrobutamine or (sandril adj2 pyronil)).mp.
- 133 (quinethazone or hydromax).mp.
- 134 Raclopride/ or (raclopride or “flb-472” or “flb 472” or “fla-870” or “fla 870” or flb472 or fla870 or “a 40664” or a40664).mp. )
- 135 Remoxipride/ or REMOXIPRIDE (nm) or (remoxipride or fla731 or “fla-731”).mp.
- 136 Reserpine/ or (reserpine or abten or alkarau or alserin or anquil or apoplom\* or austrapine or boiserpine or crystoserpin or crystoserpine or elserpine or eroseprin or eskaserp or evraloid or hiserpia or hypersine or kogluoid or lemiserp or maviserpine or “neo antitensol” or quiescin or “r-e-s” or “rau sed” or “rau-sed” or raudixoid or rauloydin or raunervil or raupina or raurine or raused or rausedan or rausedyl or rauserpine or rausingle or rautensin or rauwilid or rauwiloid or rauwolfaf or repoid or resercen or reserpamed or reserpen or reserpene or reserpex or reserpil or reserpin or reserpoid or resine or riserpa or rivasin or roxel or roxinoid or sandril or sedaraupin or serfin or serfolia or serolfia or serpalan or serpanray or serpasil or serpasol or serpate or serpen or serpena or serpentina or serpiloid or serpine or serpivite or sertabs or sertensin or sertina or “vio serpine” or “vio-serpine” or “v serp” or butiserpine or metatensin or naquival).mp.
- 137 (rimcazole or “bw 234” or “bw 234u” or bw234 or bw234u).mp.

- 138 Risperidone/ or (risperidone or belivon or consta or neripros or noprenia or "r 64766" or r64766 or "r-64766" or riperidon or risolept or rispen or risperdal or rispid or rispolet or rizodal or sequinan or zargus or zofredal).mp. (
- 139 Ritanserlin/ or RITANSERIN (nm) or (ritanserlin or "r-55667" or r55667 or "r 55667").mp.
- 140 (romergoline or "fce 23884" or fce23884 or "ls 111871" or ls111871).mp.
- 141 (savoxepine or "cgp 19486" or "cgp 19486a" or cgp19486 or cgp19486a or cipazoxapine or savoxapine).mp.
- 142 ("sb 773812" or sb773812).mp.
- 143 (seridopidine or "acr 343" or acr343).mp.
- 144 (setoperone or "r 52,245" or r 52245).mp.
- 145 Spiperone/ or Butyrophenones/ or Spiro Compounds/ or (spiperone or "r 5147" or r5147 or spiroperidol or spiroptan).mp.
- 146 (sulfuridazine or inofal or "tpn 12").mp.
- 147 Sulpiride/ or (sulpiride or tepavil or lebopride or "vertigo meresa" or pontiride or sulperide or ekilid or sulp or sulpor or "vertigo-meresa" or dolmatil or digton oe aiglonyl or guastil or sulpitil or meresa or synedil or deponerton or arminol or neogama or eglonyl or sulpivert or "vertigo-neogama" or desisulpid or psicocen or dogmatil or "vertigo neogama").mp.
- 148 (tefludazine or "lu 18 012" or "lu 18-012" or "lu 18012" or "lu18 012" or "lu18-012" or lu18012).mp.
- 149 (thiopropazate or artalan or dartal or dartalan or dartan or "sc 7105" or thiopropazat).mp.
- 150 (thiopropazine or "rp 7843" or thioperazine or majeptil or mayeptil or vontil).mp.
- 151 Thioridazine/ or (thioridazine or aldazine or apothioridazine or calmaril or mallorol or malloryl or meleril or mellaril or mellerets or mellerette\* or melleril or mellerzin or melleryl or melzine or mepiozin or orsanil or ridazin or ridazine or rideril or sonapax or thiomed or thioradazine or thioridacine or thioridazide or thioridazin or thioridazine or thioril or thiosia or thoridazine or thiozine or thioridazineneurazpharm or tioridazin or tioridazine or "tp 21" or tpzl).mp.
- 152 Thiothixene/ or (tioxixene or cis thiothixene or "cp 12,252 1" or "cp 12252 1" or "cp 122521" or "cp12,252 1" or cp12252 1 or cp122521 or navan or navane or "nsc 108165" or nsc108165 or onaven or orbinamon or "p 4657 b" or "p 4657b" or p4657b or thiotixene or thiotixin or thiotixine or thixit).mp.
- 153 Tiapride Hydrochloride/ or (tiapride or delpral or "flo 1347" or "flo-1347" or flo1347 or italprid or sereprile or thiapride or tiapridal or tiapridex or tiaprizal or equilibrium).mp.
- 154 (timiperone or "dd 3480" or dd3480 or tolopelon).mp.
- 155 ((tranylcypromine adj2 trifluoperazine) or jatrosom or parstelin or stelapar).mp.
- 156 triethylperazin\*.mp.
- 157 Trifluoperazine/ or (trifluoperazine or apotrifluoperazine or calmazine or eskazine or eskazinyl or espazine or fluoperazine or flupazine or fluperin or flurazin or "iremo-pierol" or jatroneural or leptazine or modalina or modiur or nerolet or nylipton or operzine or oxyperazine or psyrazine or "sk and f 5019" or "skf 5019" or sporalon or stelazine or terfluzin\* or triflumed or trifluoperazide or trifluoperzine or trifluperazine or trifluoroperazine or trifluorperacine or trifluorperazine or trifluperazine or triflurin or triftazin or triftazine or triftazinum or trincalm or triozine or triptazine or triphthasine or triphthazine).mp.
- 158 Trifluperidol/ or (trifluperidol or "mcn jr 2498" or psicoperidol or "r 2498" or r2498 or trifluoperidol or triperidol or trisedyl or trisedil).mp.
- 159 Triflupromazine/ or (triflupromazine or adazine or fluopromazin or fluopromazine or fluorofen or "mc 4703" or mc4703 or nivoman or psyquil or siquil or "skf 4648 a" or "skf 4648a" or skf4648a or trifluopromazine or vespral or vesprin or vetame).mp. (
- 160 (umespiron or "kc 7218" or "kc 9172" or kc7218 or kc9172).mp.
- 161 (vabicaserin or "sca 136" or sca136).mp.
- 162 (zetidoline or "dl 308" or "dl 308 it" or "dl 308it" or dl308 or dl308it).mp.
- 163 (zicronapine or "lu 31 130" or "lu 31-130" or "lu31 130" or "lu31-130").mp.
- 164 (zoloperone or "lr 511" or lr511).mp.
- 165 (zuclopenthixol or clompenthixol or cisordinol or sedanaxol or zuclopenthixol or clompixol).mp.
- 166 clonidine/ or (adesipress or arkamin or atensina or caprysin or catapres or catapresan or catasan or chlofazolin or chlophazolin or chlophelin or clonidine or clofelin or clofeline or clomidine or clondine or clonicef or clonidin or clonidine or clonipresan or clonistada or clonnirit or clophelin or clopheline or daipres or dcai or dichlorophenylaminoimidazoline or dixerit or duraclon or haemiton or hemiton or hypodine or isoglacon or jenloga or kapvay or "m 5041t" or melzin or normopresan or normopresin or paracefan or "st 155" or sulmidine or taitecin or "tenso timelet").mp.
- 167 Dexamethasone/ or (millicorten or maxidex or dexamethasone or dexpak or dexasone or oradexon or hexadecadrol or hexadrol or methylfluorprednisolone or decamet).mp.
- 168 lorazepam/ or (lorazepam or idalprem or sinestron or ativan or sedicepan or duralozam or orfidal or somagerol or apolorazepam or novolorazem or laubeel or donix or wy4036 or "wy 4036" or "wy-4036" or temesta or nuloraz or tolid).mp.
- 169 midazolam/ or (midazolam or "ro 21-3981" or "ro 21 3981" or versed or "ro 213981" or dormicum).mp.

170 diazepam/ or (diazemuls or apaurin or seduxen or faustan or sibazon or valium or stesolid or relanium).mp.  
 171 (donepezil or aricept or aricept or asenta or "e 2020" or "e2020" or eranz or memac or memorit).mp.  
 172 (rivastigmine or "ena 713" or ena713 or exelon or nimvastid or prometax or rivastigmin or "sdz 212 713" or "sdz 212-713" or "sdz 212713" or "sdz ena 713" or "sdz ena713" or "sdz212 713" or "sdz212-713" or sdz212713).mp.  
 173 or/1-172 [\*\*\*\*AntiPsychotic, benzodiazepines, cholinergic antagoists drugs - added\*\*\*\*]  
 174 Confusion/ or Psychomotor Agitation/ or hallucinations/ or illusions/ or delusions/ or paranoid behavior/ or (inattention or inattentive\*).ti,ab.  
 175 ("icu syndrome" or (intensive adj2 care adj2 unit adj2 syndrome)).ti,ab.  
 176 delirium, dementia, amnestic, cognitive disorders/ or psychotic disorders/ or delirium/  
 177 ("acute brain dysfunction" or (acute adj2 brain adj2 dysfunction\*) or "septic encephalopath\*").ti,ab.  
 178 brain diseases/ and critical illness/  
 179 brain diseases/ and sepsis/  
 180 ("acute brain failure" or "acute organic psychosyndrome\*" or "acute brain syndrome" or "metabolic encephalopath\*" or "acute psycho-organic syndrome\*" or "clouded state" or "clouding of consciousness" or "exogenous psychosis" or "toxi psychosis" or "icu psychosis").ti,ab.  
 181 brain diseases/ and (critical illness/ or Intensive Care/ or critical care/ or hospitalization/ or "length of stay"/ or patient admission/ or patient discharge/ or patient readmission/ or patient transfer/ or preoperative care/)  
 182 or/174-181 [\*\*\*\*Confusion, delirium terms\*\*\*\*]  
 183 173 and 182 [\*\*\*\*Base clinical set\*\*\*\*]  
 184 randomized controlled trial.pt.  
 185 controlled clinical trial.pt.  
 186 randomized.ab.  
 187 placebo.ab.  
 188 drug therapy.fs.  
 189 randomly.ab.  
 190 trial.ab.  
 191 groups.ab.  
 192 or/184-191  
 193 exp animals/ not humans.sh.  
 194 192 not 193 [\*\*\*\*Cochrane Handbook Highly Sensitive Search Strategy for identifying randomized trials (Box 6.4.c 2008 version)\*\*\*\*]  
 195 randomized controlled trial.pt.  
 196 controlled clinical trial.pt.  
 197 randomized.ab.  
 198 placebo.ab.  
 199 clinical trials as topic.sh.  
 200 randomly.ab.  
 201 trial.ti.  
 202 or/195-201  
 203 exp animals/ not humans.sh.  
 204 202 not 203 [\*\*\*\*Cochrane Handbook Highly Sensitive Search Strategy for identifying randomized trials (Box 6.4.d 2008 version)\*\*\*\*]  
 205 controlled clinical trial.pt. or controlled clinical trials as topic/  
 206 meta-analysis.pt. or meta-analysis as topic/  
 207 multicenter study.pt. or multicenter studies as topic/  
 208 randomized controlled trial.pt. or randomized controlled trials as topic/  
 209 tu.fs.  
 210 or/205-209 [\*\*\*\*Sensitive filter terms\*\*\*\*]  
 211 194 or 204 or 210 [\*\*\*\*Filter terms\*\*\*\*]  
 212 183 and 211 [\*\*\*\*Final results limited to trials\*\*\*\*]  
 213 183 not 212 [\*\*\*\*Non-trials\*\*\*\*] (1985)



## Appendix 2. Embase Search Strategy

Database: Embase Classic+Embase (1947 to 2017 Week 28)

Search Strategy:

- 1 antipsychotic agent/ or (antipsychotic\* or neuroleptic\* or (major adj2 (tranquilizer\* or tranquiliser\*))).mp.
- 2 aceperone/ or (aceperone or acetabutone or acetobutone or "r 3248" or r3248).mp.
- 3 acepromazine/ or acepromazine maleate/ or (acepromazine or acetopromazine or vetranquil or acetylpromazine or acepromazine or calmivet or acetazine or notensil or plegicil or promace or soprintin or anatron or anergan or atravet or "cb 1522" or cb1522 or plegicin or plegicyl or sedalin or soprintin).mp.
- 4 aceprometazine/ or (aceprometazine or acepromethazine or acetylpromethazine).mp.
- 5 acetophenazine/ or acetophenazine dimaleate/ or (acetophenazine or acephenazine or "nsc 70600" or nsc70600 or "sch 6673" or sch6673 or tindal).mp.
- 6 adopraine/ or (adopraine or adopraine or "slv 313" or slv313).mp.
- 7 alimemazine/ or alimemazine tartrate/ or (alimemazin or alimemasine or alimemazin\* or alimezine or "bayer 1219" or electrotrimeprazine or methylpromazine or palpex or "rp 6549" or rp6549 or trimeprazine or trimeprezine or varialgil or nedeltran or panectyl or repeltin or temaryl or temaryl or teralen or teralene or theralen or theralene or valergan or vallegan).mp.
- 8 "alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol"/ or ("bms 181100" or bms181100 or "bmy 14802" or "bmy 14802 1" or "bmy 14802-1" or bmy14802 or "bmy14802 1" or "bmy14802-1" or bmy148021).mp.
- 9 "alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol"/ or ("bms 181100" or bms181100 or "bmy 14802" or "bmy 14802 1" or "bmy 14802-1" or bmy14802 or "bmy14802 1" or "bmy14802-1" or bmy148021).mp.
- 10 "alpha [1 [2 (1,4 benzodioxan 5 yloxy)ethyl] 3 pyrrolidinyl] 4 fluoroacetophenone"/ or ("s 16924" or s16924).mp.
- 11 amitriptyline plus perphenazine/ or amitriptyline perphenazine/ or ((amitriptyline adj2 perphenazine) or "anxipress-d" or "duo-vil 2-10" or "duo-vil 2-25" or "duo-vil 4-10" or etrafon or etrafon or longopax or mutabon or mutanxion or mutaspine or "neuragon-a" or "neuragon-b" or pertriptyl or polybon or triavil or triptafen).mp.
- 12 aplindore/ or (apindore or "dab 452" or dab452 or palindore or "way dab 452" or "way dab452").mp.
- 13 atypical antipsychotic agent/ or (atypical adj2 (antipsychotic\* or neuroleptic\*)).mp. or "1 cyclopropylmethyl 4 [2 (4 fluorophenyl) 2 oxoethyl]piperidine"/ or "1,2,3,4,8,9,10,10a octahydro 7bh cyclopenta[b][1,4]diazepino[6,7,1 hi]indole"/ or "2 amino n [4 [4 (1,2 benzisothiazol 3 yl) 1 piperazinyl]butyl]benzamide"/ or "2 chloro 11 (3 dimethylaminopropylidene)morphanthridine"/ or "4 (4 fluorophenyl) 1,2,3,6 tetrahydro 1 [4 (1,2,4 triazol 1 yl)butyl]pyridine"/ or "4,9 dibromo 6 (4 methyl 1 piperazinyl)benzo[b]pyrrolo[3,2,1 jk][1,4]benzodiazepine"/ or "7 [3 [4 (2,3 dimethylphenyl) 1 piperazinyl]propoxy] 2(1h) quinolinone"/ or "7 chloro 2 [[1 (2 methoxyphenyl) 4 piperidyl]methylaminomethyl] 1,4 benzodioxan"/ or "8 fluoro 4 [3 (2 methoxyethyl) 4 methyl 1 piperazinyl] 2 methyl 10h thieno[2,3 b][1,5]benzodiazepine"/
- 14 atypical antipsychotic agent/ or (atypical adj2 (antipsychotic\* or neuroleptic\*)).mp. or abaperidone/ or (abaperidone or "fi 8602" or fi8602).mp. or alentamol/ or (alentamol or alentemol or "u 66444b" or "u 68552b" or "u 68553b" or u66444b or u68552b or u68553b).mp. or amisulpride/ or (aminosultopride or amisulpride or amisulpridum or "dan 2163" or dan2163 or sertol or solian).mp. or amperozide/ or (amperozide or "fg 5606" or fg5606).mp. or aripiprazole/ or (aripiprazole or abilify or abilitat or "opc 14597" or opc14597).mp. or asenapine/ or (asenapine or "org 5222" or org5222 or saphris or sycrest).mp. or batelapine/ or (batelapine or "cgs 13429" or cgs13429).mp. or belaperidone/ or (belaperidone or balaperidone or "lu 111995" or lu111995).mp. or bifeprunox/ or (bifeprunox or "du 127090" or du127090).mp. or elopiprazole/ or emonapride/ or (emonapride or emirace or nemonapride or "ym 09151" or "ym 09151 02" or "ym 09151 2" or "ym 09151-02" or "ym 09151-2" or ym09151 or "ym09151 02" or "ym09151 2" or "ym09151-02" or "ym09151-2" or ym0915102 or ym091512).mp. or flumetazepam/ or (flumetazepam or "ly 120363" or ly120363).mp. or fluoxetine plus olanzapine/ or ((fluoxetine adj2 olanzapine) or symbyax).mp. or fluperlapine/ or (fluperlapine or "nb 106689" or nb106689).mp. or iloperidone/ or (iloperidone or fanapt or fanaptum or "hp 873" or hp873 or "ilo 522" or ilo522 or zomaril).mp. or lurasidone/ or (lurasidone or latuda or "mk 3756" or mk3756 or "sm 13496" or sm13496 or "smp 13496" or smp13496).mp. or melperone/ or (melperone or bunil or buronil or eunerpan or "fg 5111" or fg5111 or flubuperone or melperon or methylperone or metylperone or metylperonum).mp. or "n (2 chloro 6 methylergolin 8alpha yl)pivalamide"/ or ("sdz 208 912" or "sdz 208-912" or "sdz 208912" or "sdz 912" or "sdz hdc 912" or "sdz hdc912" or "sdz208 912" or "sdz208-912" or sdz208912 or sdz912).mp. or "n (2,6 dimethylergolin 8alpha yl)pivalamide"/ or ("sdz 208 911" or "sdz 208-911" or "sdz 208911" or "sdz 911" or "sdz hac 911" or "sdz hac911" or "sdz208 911" or "sdz208-911" or sdz208911 or sdz911).mp. or "n cyclohexyl 4 [4 (4 fluorophenyl) 4 oxobutyl] 1 piperazinecarboxamide"/ or ("fg 5803" or fg5803).mp. or norclozapine/ or (norclozapine or demethylclozapine or desmethylclozapine).mp. or ocaperidone/ or (ocaperidone or "r 79598" or r79598).mp. or olanzapine/ or (olanzapine or anzatric or "dopin tab" or "jolyon md" or lanopin or lanzac or "ly 170053" or ly170053 or meltolan or midax or olace or oladay or olan or olandus or olanex or olansek or olapin or olazax or oleanz or olexar or oltal or olzap or onza or "ozapin md" or psychozap or relprev or

zalasta or zelta or zydis or zypadhera or zyprex or zyprexa or zyprexav).mp. or paliperidone/ or (paliperidone or invega or "paliperidone palmitate" or "r 76477" or r76477 or "ro 76477" or "ro 92670" or ro76477 or ro92670 or xelplion).mp. or panamesine/ or (panamesine or "emd 57445" or emd57445).mp. or pentiapine/ or pentiapine maleate/ or (pentiapine or "cgs 10746" or cgs10746 or "cgs 10746b" or cgs10746b).mp. or perlapine/ or (perlapine or "aw 14'2333" or "aw 142333" or aw142333 or perlapin).mp. or perospirone/ or (perospirone or lullan or "sm 9018" or sm9018).mp. or pridopidine/ or (pridopidine or "acr 16" or acr16 or "asp 2314" or asp2314 or "fr 310826" or fr310826 or huntexil).mp. or quetiapine/ or (quetiapine or "ici 204636" or "ici 204646" or ici204636 or ici204646 or seroquel or socalm or tienapine).mp. or remoxipride/ or (remoxipride or "a 33547" or a33547 or "fla 731" or fla731 or roxiam).mp. or rilapine/ or rilapine.m.p. or sertindole/ or (sertindole or "lu 23174" or lu23174 or "s 1991" or s1991 or serdolect or serlect).mp. or sulpiride/ or (sulpiride or abilit or aiglonyl or arminol or dobren or dogmatil or dogmatyl or dolmatil or eglonil or equilid or "fk 880" or fk880 or isnamide or levobren or levopraid or levosulpiride or meresa or miradol or neogama or sulfiride or sulpivot or sulpyride or synedil or vipral).mp. or sultopride/ or (sultopride or barnetil or barnotil or "ms 5024" or ms5024 or sulfopride).mp. or tenilapine/ or tenilapine.m.p. or tiospirone/ or (tiospirone or "bmy 13859" or bmy13859 or "mj 13859" or "mj 13859 1" or "mj 13859-1" or mj13859 or "mj13859 1" or "mj13859-1" or mj138591 or tiaspirone).mp. or volinanserine/ or (volinanserine or "m 100907" or m100907 or "mdl 100151" or "mdl 100907" or mdl100151 or mdl100907).mp. or ziprasidone/ or (ziprasidone or "cp 88059" or "cp 88059 01" or "cp 88059 27" or "cp 88059-01" or "cp 88059-27" or "cp 8805901" or "cp 8805927" or cp88059 or "cp88059 01" or "cp88059 27" or "cp88059-01" or "cp88059-27" or cp8805901 or cp8805927 or geodon or zeldox or zeldrox or zipsydon).mp. or zotepine/ or (zotepine or lodopin or nipolept).mp.

15 azaperone/ or (azaperone or "r-1929" or r1929 or sedaperone or stresnil).mp.

16 benperidol/ or (benperidol or anquil or benperidone or benzoperidol or benzperidol or benperidolneuraxpharm or "cb 8089" or cb8089 or frenactyl or frenactil or glanimon or "mcn jr 4584" or "mcn jr4584" or phenactil or "r 4584" or r4584).mp.

17 berupipam/ or (berupipam or "nnc 22 0010" or "nnc22 0010").mp. (8)

18 bitopertin/ or (bitopertin or paliflutine or "r 1678" or r1678 or "rg 1678" or rg1678 or "ro 4917838" or ro4917838).mp.

19 blonanserine/ or (blonanserine or "ad 5423" or ad5423 or lonasen).mp.

20 brexpiprazole/ or (brexpiprazole or "opc 34712" or opc34712).mp.

21 brofoxine/ or (brofoxine or dimetabrone or "fi 6820" or fi6820).mp.

22 bromospiperone/ or (bromospiperone or bromospiroperidol).mp.

23 bromperidol/ or bromperidol decanoate/ or (bromperidol or impromen or "r 11,333" or "r 11333" or "r11,333" or r11333 or tesoprel or "impromen decanoate" or "r 46,541" or "r 46541" or "r46,541" or r46541).mp.

24 butaclamol/ or ("ay 23,028" or "ay 23028" or "ay23,028" or "ay-23028" or ay23028 or butaclamol).mp.

25 butaperazine/ or (butaperazine or "ahr 3000" or "bayer 1362" or butaperazinum or butyrylperazin or butyrylperazine or megalactil or randolectil or randolectyl or repoise or "riker 595" or tyrylen).mp.

26 carfenazine/ or (carfenazine or carfenazinum or carphenazine or "nsc 71755" or nsc71755 or procethazine or proketazine or "wy 2445" or wy2445).mp.

27 cariprazine/ or (cariprazine or "mp 214" or mp214 or "rgh 188" or rgh188).mp.

28 carpipramine/ or (carpipramine or carbadipimidine or defecton or defekton or prazinil or "pz 1511" or pz1511 or "rp 21679" or rp21679).mp.

29 carvotroline/ or (carvotroline or "wy 47791" or wy47791).mp. (7)

30 centbutindole/ or centbutindole.m.p.

31 chlorothiazide plus reserpine/ or (chlorothiazide or "diupres-250" or "diupres-500").mp.

32 chlorphenethazine/ or (chlorphenethazine or chlorfenethazine or elroquil or marophen).mp.

33 chlorproethazine/ or (chlorproethazine or neuriplege or "rp 4909" or rp4909).mp.

34 chlorpromazine/ or chlorpromazine plus dexamphetamine/ or chlorpromazine sulfoxide/ or (chlorpromazine or "2601 a" or "4560 r p" or aminasin or aminasine or aminazin or aminazine or ampliactil or ampticil or ancholactil or aspersinal or bellacina or cepezet or chlomazine or "chlor pz" or chloractil or chlorazine or chlorbromasin or chlorderazine or chlorderazin or chlormazine or chlorpromanyl or chlorpromazin or chlorpromed or clonazine or clordelazin or clorpromaz or clorpromazine or clozine or contomin or duncan or elmarin or esmino or fenactil or hibanil or hibernal or hibernal or "hl 3746" or "hl 5746" or klorproman or klorpromazin or klorpromex or laractyl or largactil or largactyl or matcine or megaphen or megatil or "ml 5746" or neomazine or neurazine or novomazina or phenathyl or plegomazin or plegomazine or proma or promacid or promactil or promapar or promazil or promexin or propaphen or propaphenin or prozil or prozin or psychazine or psynor or "rp 4560" or sanopron or "skf 2601 a" or solidon or sonazine or taroctil or taroctyl or "thor prom" or thorazene or thorazine or torazina or "vegetamin a" or "vegetamin b" or winsumin or wintamine or wintermin or zuledin or "thora-dex" or opromazine or secotil).mp.

35 cinuperone/ or (cinuperone or "hr 375" or hr375).mp.

36 clocapramine/ or (clocapramine or "y 4153" or y4153).mp.

37 cloflumide mesilate/ or ("cloflumide mesylate" or "vufb 15496" or vufb15496).mp.

38 clofluperol/ or (clofluperol or seperidol).mp.

39 clompenthixol/ or clompenthixol decanoate/ or (clompenthixol or "ay 62021" or ay62021 or chlorpenthixol or chlorperphenthixene or chlorperphenthixene or ciatyl or cisordinol or clompenthixol or cloxipol or "n 746" or n746 or "nsc 64087" or nsc64087 or sordinol or zuclopenthixol).mp.

40 clomozide/ or (clomozide or "r 29,764" or "r 29764" or "r29,764" or r29764).mp. )

41 clomipazan/ or (clomipazan or "skf 69634" or skf69634).mp.

42 clomipramine/ or (clomipramine or cremin or mosapramine or "y 516" or y516).mp.

43 clotiapine/ or (clotiapine or clothiapin or clothiapine or entumin or entumine or etumine or "hf 2159" or hf2159).mp.

44 cp 903397/ or ("cp 903397" or cp903397).mp.

45 cryptenamine plus reserpine/ or (cryptenamine or "unitensen-r").mp.

46 (cryptenamine or "unitensen-r").mp.

47 clozapine/ or clozapine derivative/ or clozapine n oxide/ or (alemoxan or azaleptin or clopine or clapsine or clozapin\* or clozaril or denzapine or dorval or rdopazine or elcrit or fazaclo or "hf 1854" or hf1854 or lapenax or leponex or lozapin\* or sizopin or versacloz or "wander compound" or zapen or zaponex).mp.

48 cyamemazine/ or (cyamemazine or cianatil or cyamepromazine or "fi 6229" or fi6229 or kyamepromazin or "rp 7204" or rp7204 or tercián).mp.

49 dexamphetamine plus prochlorperazine/ or ((dextroamphetamine adj2 sulfate adj2 prochlorperazine) or "eskatrol spansule").mp.

50 dexamphetamine plus reserpine/ or ((dexamphetamine or dexserpine or dextroamphetamine) adj2 reserpine).mp.

51 diethylstilbestrol plus methyltestosterone plus reserpine/ or ((diethylstilbestrol adj2 methyltestosterone) or tylandril).mp.

52 dimetotiazine/ or (dimetotiazine or banistyl or dimethiotiazine or dimethiothazine or dimethothiazine or dimethotiazine ro dime-tiotiazine or fonazine or "il 6302").mp.

53 dimevamide plus phenobarbital plus reserpine/ or ((dimevamide adj2 phenobarbital) or "neuro-centrine tablet\*").mp.

54 dixyrazine/ or (dixyrazine or dixirazine or dixyrazin or dyxirazine or esocalm or esucos or metronal or roscal or "ucb 3412" or ucb3412).mp.

55 dolasetron mesilate/ or (dolasetron or anemet or anzemet or "mdl 73147" or "mdl 73147ef" or mdl73147 or mdl73147ef or zamanon).mp.

56 droperidol/ or droperidol plus fentanyl/ or droperidol plus fentanyl citrate/ or (droperidol or dehidrobenzoperidol or dehydroben-zoperidol or dehydrobenzoperiol or dehydrobenzperidol or dehydrobenzperidolum or dridol or droleptan or droperol or halkan or inaprine or inapsin or inapsine or "mcn jr 4749" or "mcn r 4749" or oridol or "r 4749" or sintodian or troperidol or xomolix or innovan or innovar or inoval or inovar or talamonal or thalamonal or disifelit).mp.

57 duoperone/ or (duoperone or "ahr 6646" or ahr6646).mp.

58 ephedrine sulfate plus reserpine/ or ((ephedrine adj2 sulfate) or renir).mp.

59 ethinylestradiol plus reserpine/ or ((ethinylestradiol adj2 reserpine) or estrosed or sergynol).mp.

60 etymemazine/ or (etymemazine or diquel or ethotrimprazine or ethylisobutrazine or ethymemazine or nualt or "rp 6484" or rp6484 or sergetyl).mp.

61 (etazolate or sq20009 or "sq-20009" or "sq 20009").mp. (257)

62 farampator/ or (farampator or "cx 691" or cx691 or "org 24448" or org24448).mp.

63 fluanisone/ or (fluanisone or "anti pica" or antipica or fluanison\* or fluanizone or fluoanisone or haloanison or haloanisone or "md 2028" or md2028 or "r 2028" or "r 2167" or r2028 or r2167 or sedalande or sedalanide or solusediv).mp. )

64 flupentixol/ or flupentixol decanoate/ or (flupentixol or flupenthixol\* or emergil or fluanxol or fluxanxol or "lc 44" or lc44 or "n 7009" or n7009 or siplaryl or siplaryl or depixol or depot or "lu 5 110" or "lu 5110" or viscoleo).mp.

65 fluphenazine/ or fluphenazine decanoate/ or fluphenazine enanthate/ or (fluphenazin\* or anatensil or anatensol or antasol or cenilene or dapotum or elinol or flufenan or flufenazine or flumezin or fluorfenazine or fluphenacin or "fluzine-p" or ftorphenazine or "luogen depot" or lyogen or lyorodin or moditen or moditin or omca or pacinol or permitil or phthorphenazine or potensone or prolixan or prolixene or prolixin\* or "s 94" or sevinol or sevinol or squaline or squalon\* or siquoline or "sq 4918" or sq4918 or tensofin or trancin or valamina or vespazin\* or "dapatum d25" or dapotum or decafen or flucan or fludecasine or fludecate or lyogen or mirenil or modocate or phlufdek or sydepres or flunanthate).mp.

66 fluspirilene/ or (fluspirilene or fluspi or fluspirilen or imap or "mcn jr 6218" or "mcn jr6218" or "r 6218" or r6218 or redeptin or spirodiflamine or kivat).mp.

67 flutroline/ or (flutroline or "cp 36,584" or "cp 36584" or "cp36,584" or cp36584).mp.

68 "gamma endorphin[deenkephalin]" or ((endorphin adj2 deenkephalin) or "beta endorphin[6-17]" or "beta lipotropin[66-77]" or "org 5878" or org5878).mp.

69 gevetroline/ or (gevetroline or “wy 47384” or wy47384).mp.

70 glyceryl trinitrate plus pentaerythrityl tetranitrate plus reserpine/ or penite.mp.

71 haloperidol/ or haloperidol decanoate/ or (haloperidol or alased or aloperidin\* or avant or binison or brotopon or celenase or cereen or cerenace or cizoren or depidol or dores or dozic or duraperidol or “einalon s” or fortunat or govotil or haldol or halidol or “halo-p” or halojust or halomed or haloneural or haloper or haloperil or haloperin or haloperitol or halopidol or halopol or halosten or haricon or “haridol-d” or keselan or linton or “lodomer-2” or “mcn jr 1625” or “mcn jr1625” or mixidol or novoperidol or “nsc 170973” or nsc170973 or peluces or perida or peridol or peridor or “r 1625” or r1625 or selezyme or seranace or serenase or serenase or serenelfi or siegoperidol or sigaperidol or trancodol or pericate or “r 13,672” or “r 13672” or senorm).mp.

72 hexamethonium chloride plus reserpine/ or reserthonium.mp.

73 hydralazine plus reserpine/ or hydrochlorothiazide plus potassium chloride plus reserpine/ or hydrochlorothiazide plus reserpine/ or (dralserp or (hydralazine adj2 reserpine) or “serpasil-apresoline” or hydropres or “dichlotride s” or “h.r.-50” or “hydro-reserp” or hydrochlorothiazide or hydroserpine or “medeserpine co” or “serpasil-esidrix”).mp.

74 hydrochlorothiazide plus reserpine plus secbutabarbital/ or ((hydrochlorothiazide adj2 reserpine adj2 secbutabarbital) or butiserpazide).mp.

75 hydroflumethiazide plus potassium chloride plus reserpine/ or ((hydroflumethiazide adj4 reserpine) or rautrax).mp. )

76 hydroflumethiazide plus reserpine/ or ((hydroflumethiazide adj2 reserpine) or salutensin\*).mp.

77 isofloxythepin/ or (isofloxythepin or “vufb 10662”).mp.

78 isomolpan/ or (isomolpan or “cgs 15855” or “cgs 15855 a” or “cgs 15855a” or cgs15855 or cgs15855a).mp.

79 isopropamide iodide plus prochlorperazine maleate/ or ((isopropamide adj4 prochlorperazine) or “combid spansule”).mp.

80 lenperone/ or (lenperone or “ahr 2277” or ahr2277 or elanone).mp.

81 levomepromazine/ or (levomepromazine or “apo-methoprazine” or “bayer 1213” or “cl 36467” or “cl 39743” or cl36467 or cl39743 or hiranamin or mepromazine or levium or promazine or levomeprazine or levopromazin\* or levoprome or levozin or mepromazine or methotrimprazine or methozane or milezin or minozinan or neozine or neuractil or neurocil or nirvan or nozinan or “rp 7044” or rp7044 or sinogan or “sk and f 5116” or “skf 5116” or skf5116 or tiscerin or tiscerin or veractil).mp.

82 lithium/ or lithium.mp.

83 loxapine/ or loxapine succinate/ or (loxapine or adasuve or “alxz 004” or alxz004 or “az 004” or az004 or “cl 62,362” or “cl 62362” or “cl62,362” or cl62362 or “cl 71563” or “cl-71563” or cl71563 or loxapinsuccinate or cloxazepin\* or loxapane or loxapin\* or loxitane or oxilapine or “sum 3170” or sum3170 or daxolin or desconex or loxapac).mp.

84 maroxepine/ or maroxepine.mp.

85 mazapertine/ or (mazapertine or “rwj 37796” or rwj37796).mp.

86 mepiprazole/ or meprobamate plus promazine/ or (mepiprazole or “emd 16923” or emd16923 or psigodal or prozine or meprobamate).mp.

87 mesoridazine/ or mesoridazine besylate/ or (mesoridazin\* or esoridazine or lidanar or lidanil or mesorin or “nc 123” or (thioridazine adj2 sulfoxide) or “tps 23” or serentil).mp.

88 methamphetamine plus reserpine/ or ((methamphetamine adj2 reserpine) or “du-oria”).mp.

89 methyclothiazide plus reserpine/ or (methiothepin\* or metitepine or “diutensen-r”).mp.

90 methopromazine/ or (methopromazine or methoxypromazine or metopromazine).mp.

91 (levopromazine or tizercine or methotrimprazine or levomepromazine or levomeprazin or tiscerin or tizertsin).mp.

92 metofenazate/ or (metofenazate or frenolon or metaphenazine or methophenazine or metophenazine or phrenolon).mp.

93 molindone/ or (molindon\* or “en 1733a” or en1733a or lidone or moban or molindor).mp.

94 moperone/ or (moperone or luvaten or luvarena or “methyl peridol” or methylperidol\* or moperon or “r 1658”).mp.

95 “n [(1 butyl 2 pyrrolidinyl)methyl] 2,3 dihydro 2 methyl 5 sulfamoyl 7 benzofurancarboxamide”/ or (“y 20024” or y20024).mp.

96 “n [3 (4 fluorophenyl) 3 (4 phenylphenoxy)propyl]sarcosine”/ or (“alx 5407” or alx5407 or NFPS).mp.

97 “n [4 [2 (6 cyano 1,2,3,4 tetrahydro 2 isoquinolinyl)ethyl]cyclohexyl] 4 quinolinecarboxamide”/ or (“sb 277011” or “sb 277011a” or sb277011 or sb277011a).mp.

98 neboglamine/ or (neboglamine or “cr 2249” or cr2249 or “xy 2401” or xy2401).mp.

99 nicotinic acid plus pentetrazole plus reserpine/ or ((nicotinic adj4 pentetrazole adj4 reserpine) or (nicozol adj2 reserpine)).mp. (1)

100 noctran/ or noctran.mp.

101 norchlorpromazine/ or (norchlorpromazine or demethylchlorpromazine or demonomethylchlorpromazine or desmethylchlorpromazine or desmonomethylchlorpromazine or monodesmethylchlorpromazine).mp.

102 Ondansetron/ or (ondansetron or gr38032f or “gr 38032f” or “sn 307” or sn307 or “gr-38032f” or “sn-307” or zofran).mp.

103 oxiperomide/ or (oxiperomide or “r 4714” or r4714).mp.

- 104 oxypertine/ or (oxypertin\* or “cl 77328” or cl77328 or equipertine or forit or opertil or oxipertin or oxypertin or “win 18501 2” or “win 18501-2” or “win 185012” or “win18501 2” or “win18501-2” or win185012).mp.
- 105 oxyprothepine/ or oxyprothepine decanoate/ or (oxyprothepine or oxyprothepin).mp.
- 106 pecazine/ or (pecazine or lacumin or mepasin or mepazine or nothiazine or “p 391” or pacatal or pacatol or pactal or papital or paxital or pecazine or “w 1224”).mp.
- 107 penfluridol/ or (penfluridol or “mcn jr 16,341” or “mcn jr 16341” or micefal or “r 16,341” or “r 16341” or semap or “r 16341” or “r-16341” or r16341).mp.
- 108 Perazine/ or (perazine or taxilan).mp.
- 109 (pentaerythrityl or pentaserpine or respet or pentraline).mp.
- 110 pentaerythrityl tetranitrate plus reserpine/ or pentaerythrityl tetranitrate plus reserpine plus secbutabarbitol/ or (pentaerythrityl or pentaserpine or respet or pentraline).mp.
- 111 pentobarbital plus reserpine/ or (“nembu-serpine” or (pentobarbital adj2 reserpine)).mp.
- 112 perazine/ or (perazine or “p 725” or pernazine or taxilan).mp.
- 113 periciazine/ or (periciazine or aolept or neulactil or neuleptil\* or periciazinum or pericyazine or properciazine or propericiazin or propericiazine or “rp 8909” or “skf 20716”).mp.
- 114 perimetazine/ or (perimetazine or “1317 an” or “an 1317” or an1317 or lepryl or perimethazine).mp.
- 115 perphenazine/ or perphenazine decanoate/ or perphenazine enanthate.m. or (perphenazine or chlorperphenazine or chlorpiprazine or chlorpiprozine or decentan or etaperazine or ethaperazine or “f-mon” or fentazin or leptopsique or peratsin or perfenazine or perforazine or pernamed or perphenan or perphenazin\* or “perzine-p” or porazine or “sch 3940” or thilatazin or tranquisan or trifalon or trilafan or trilafon or trilifan or triliphan or triomin).mp.
- 116 (“pf 217830” or pf217830 or “pf 2400013” or pf2400013 or “pf 3463275” or pf3463275).mp.
- 117 phenobarbital plus reserpine/ or phenobarbital plus reserpine plus theobromine/ or phenobarbital plus reserpine plus thiamine.m. or ((phenobarbital adj2 reserpine) or “solfo-serpine” or bromoserpin or “theo-serp” or “theobarb-r” or theoserpin or besertal or “neo-slowten”).mp.
- 118 picobenzide/ or (picobenzide or dosetil or “m 14012 4” or “ma 14012” or picobenzamide).mp.
- 119 piflutixol/ or piflutixol.m.
- 120 pimavanserine/ or (pimavanserine or “acp 103” or acp103).mp. (172)
- 121 pimethixene/ or (pimethixene or “bp 400” or “bp 400 e” or “bp 400e” or bp400 or bp400e or muricalm or pimetixin).mp.
- 122 pimozone/ or (pimozone or antalon or “mcn jr 6238” or opiran or orap or pimocide or pimoride or pinozone or pizide or “r 6238” or r6238).mp.
- 123 pipamperone/ or (pipamperone or dipeperon or dipiperon or “dl piperonyl” or floropipamide or “piperonyl of pripamperone of r 3345” or r3345).mp.
- 124 piperacetazine/ or (piperacetazine or “pc 1421 or pc1421” or guide).mp.
- 125 pipotiazine/ or pipotiazine palmitate/ or pipotiazine undecenoate/ or (pipotiazine or “9366 rp” or piportil or pipothiazine or “rp 19366” or rp19366 or “il 19552” or il19552 or “rp 19552” or rp19552 or rp 19551).mp.
- 126 pirenperone/ or polythiazide plus reserpine/ or (pirenperone or “r 47,465” or “r 47465” or “r 50656” or “r47,465” or r47465 or r50656 or “renese r” or “renese-r”).mp.
- 127 pomaglutetad methionil/ or (“pomaglutetad methionil” or “ly 2140023” or ly2140023).mp.
- 128 prochlorperazine/ or prochlorperazine edisylate/ or prochlorperazine maleate/ or (prochlorperazine or “6140 rp” or antinaus or “bayer a 173” or “bayer 173” or capazine or chlormepazine or chlorpeazine or chlorperazine or compro or dicopal or emelent or klometil or kronocin or meterazine or metherazine or nautisol or nipodal or normalmin or pasotomin or prochlor or prochlorpemazine or prochlorperazine or prochlorperazine or prochlorpromazine or prochlorperazine or procot or “rp 6140 ir rp6140” or “sk and f 4657” or “skf 4657” or skf4657 or temetil or temetil or buccastem or dhaperazine or emeteral or emetiral or nibromin or proclozine or procomp or stemetil or stemzine).mp.
- 129 profenamine/ or (profenamine or dibutil or ethopropazine or etopropazine or isothazine or isothiazine or lysivane or parcidol or pardisol or parfezin\* or parkisol or parphezin or parsidol or parsitan or phenopropazine or “profenamine hydrochloride” or prophenamine or rochipel or rodipal or “rp 3356” or “sc 2538”).mp.
- 130 promazine/ or (promazine or alofen or alophen or ampazine or amprazim or centractyl or delazin or esparin or lete or liranol or “neo hibernex” or neuroplegil or piarine or prazine or “pro tan” or promantine or promanyl or promilene or promwill or protactil or protactyl or romthiazine or romtiazin or “rp 3276” or sediston or sinophenin\* or sparine or tomil or varophen or verophen or “wy 1094”).mp. (3625)
- 131 propantheline bromide plus thiopropazate/ or ((propantheline adj4 thiopropazate) or “pro-banthine”).mp.

- 132 propiomazine/ or propiomazine maleate/ or (propiomazine or “cb 1678” or cb1678 or largon or propionylpromethazine or propriomazine or propromazine or dorevane or indorm or phenoctyl or propavan or “wy 1359”).mp.
- 133 propionylpromazine/ or (propionylpromazine or combelen or dipropiomazine or propiopromazine or tranvet).mp.
- 134 prothipendyl/ or (prothipendyl or “ay 5603” or ay5603 or azacon or “d 206” or d206 or dominal or inalforte or largophren or “lg 206” or lg206 or phrenotropin or prothipendil or protipendil or protipendyl or timovan or tolnate or tumovan).mp.
- 135 protoveratrine A plus protoveratrine B plus reserpine/ or protoveratrine A plus reserpine/ or pyrrobutamine plus reserpine/ or (protoveratrine or “veralba r” or verapene or “protalba-r” or pyrrobutamine or (sandril adj2 pyronil)).mp.
- 136 quinethazone plus reserpine/ or hydromax.mp.
- 137 raclopride/ or raclopride tartrate/ or (raclopride or “flb-472” or “flb 472” or “fla-870” or “fla 870” or flb472 or fla870 or “a 40664” or a40664).mp.
- 138 Remoxipride/ or (remoxipride or fla731 or “fla-731”).mp.
- 139 reserpine/ or reserpine plus secbutabarbitol/ or reserpine plus trichlormethiazide/ or (reserpine or abten or alkarau or alserin or anquil or apoplon\* or austrapine or boiserpine or crystoserpin or elserpine or eroseprin or eskaserp or evraloid or hiserpia or hypersine or koglucoïd or lemiserp or maviserp or “neo antitensol” or quiescin or “r-e-s” or “rau sed” or “rau-sed” or raudixoid or rauloydin or raunervil or raupina or raurine or roused or rousedan or rousedyl or rauserpine or rausingle or rautensin or rauwilid or rauwiloid or rauwolfaf or repoid or resercen or reserpamed or reserpen or reserpene or reserpex or reserpil or reserpin or reserpoid or resine or riserpa or rivasin or roxel or roxinoid or sandril or sedaraupin or serfin or serfolia or serolfia or serpalan or serpanray or serpasil or serpasol or serpate or serpen or serpena or serpentina or serpiloid or serpine or serpivite or sertabs or sertensin or sertina or “vio serpine” or “vio-serpine” or butiserpine or metatensin or naquival).mp.
- 140 rimcazele/ or (rimcazele or “bw 234” or “bw 234u” or bw234 or bw234u).mp.
- 141 risperidone/ or (risperidone or belivon or consta or neripros or noprenia or “r 64766” or r64766 or “r-64766” or riperon or risolept or rispen or risperdal or rispil or rispolet or rizodal or sequinan or zargus or zofredal).mp.
- 142 Ritanserine/ or (ritanserine or “r-55667” or r55667 or “r 55667”).mp.
- 143 romergoline/ or (romergoline or “fce 23884” or fce23884 or “ls 111871” or ls111871).mp.
- 144 savoxepine/ or (savoxepine or “cgp 19486” or “cgp 19486a” or cgp19486 or cgp19486a or cipazoxapine or savoxapine).mp. (38)
- 145 (“sb 773812” or sb773812).mp.
- 146 seridopidine/ or (seridopidine or “acr 343” or acr343).mp. (2)
- 147 setoperone/ or (setoperone or “r 52,245” or r 52245).mp. (193)
- 148 spiperone/ or (spiperone or “r 5147” or r5147 or spioperidol or spiropitan).mp.
- 149 sulforidazine/ or (sulforidazine or inofal or “tpn 12”).mp.
- 150 Sulpiride/ or (sulpiride or tepavil or lebopride or “vertigo meresa” or pontiride or sulperide or ekilid or sulp or sulpor or “vertigo-meresa” or dolmatil or digton oe aiglonyl or guastil or sulpitil or meresa or synedil or deponerton or arminol or neogama or eglonyl or sulpivert or “vertigo-neogama” or desisulpilid or psicocen or dogmatil or “vertigo neogama”).mp.
- 151 tefludazine/ or (tefludazine or “lu 18 012” or “lu 18-012” or “lu 18012” or “lu18 012” or “lu18012”).mp.
- 152 tepirindole/ or (tepirindole or “hr 592” or hr592 or “ru 27592” or ru27592).mp.
- 153 thiopropazate/ or (thiopropazate or artalan or dartal or dartalan or dartan or “sc 7105” or thiopropazat).mp.
- 154 thioproperazine/ or thioproperazine methanesulfonate/ or (thiopropazine or “rp 7843” or thioperazine or majeptil or mayeptil or vontil).mp.
- 155 thioridazine/ or (thioridazine or aldazine or apothioridazine or calmaril or mallorol or malloryl or meleril or mellaril or mellerets or mellerette\* or melleril or mellerzin or melleryl or melzine or mepiozin or orsanil or ridazin or ridazine or rideril or sonapax or thiomed or thioradazine or thioridacine or thioridazide or thioridazin or thioridazine or thioril or thiosia or thioridazine or thiozine or thioridazineneurazpharm or tiordazin or tiordazine or “tp 21” or tpzl).mp.
- 156 tiotixene/ or (tiotixene or cis thiothixene or “cp 12,252 1” or “cp 12252 1” or “cp 122521” or “cp12,252 1” or cp12252 1 or cp122521 or naven or navane or “nsc 108165” or nsc108165 or onaven or orbinamon or “p 4657 b” or “p 4657b” or p4657b or thiotixene or thiotixin or thiotixine or thixit).mp.
- 157 Tiapride/ or (tiapride or delpal or “flo 1347” or “flo-1347” or flo1347 or italprid or sereprile or thiapride or tiapridal or tiapridex or tiaprizal or equilibrium).mp.
- 158 timiperone/ or (timiperone or “dd 3480” or dd3480 or tolopelon).mp.
- 159 tranlycypromine plus trifluoperazine/ or ((tranlycypromine adj2 trifluoperazine) or jatrosom or parstelin or stelapar).mp.
- 160 triethylperazine/ or triethylperazin\*.mp.
- 161 trifluoperazine/ or trifluoperazine derivative/ or (trifluoperazine or apotrifluoperazine or calmazine or eskazine or eskazinyl or espazine or fluoperazine or flupazine or fluperin or flurazin or “iremo-pierol” or jatroneural or leptazine or modalina or modiuor or nerolet or nylipton or operzine or oxyperazine or psyrazine or “sk and f 5019” or “skf 5019” or sporalon or stelazine or terfluzin\* or

triflumed or trifluoperazide or trifluoperzine or trifluperazine or trifluoroperazine or trifluorperacine or trifluorperazine or trifluperazine or triflurin or triflazin or triftazine or triftazinum or trincalm or triozone or triptazine or triphthasine or triphthazine).mp.

162 trifluoperidol/ or (trifluoperidol or "mcn jr 2498" or psicoperidol or "r 2498" or r2498 or trifluoperidol or triperidol or trisedyl or trisedil).mp.

163 triflupromazine/ or (triflupromazine or adazine or fluopromazin or fluopromazine or fluorofen or "mc 4703" or mc4703 or nivoman or psyquil or siquil or "skf 4648 a" or "skf 4648a" or skf4648a or trifluopromazine or vespral or vesprin or vetame).mp.

164 umespirone/ or (umespirone or "kc 7218" or "kc 9172" or kc7218 or kc9172).mp.

165 vabicaserin/ or (vabicaserin or "sca 136" or sca136).mp.

166 zetidoline/ or (zetidoline or "dl 308" or "dl 308 it" or "dl 308it" or dl308 or dl308it).mp.

167 zicronapine/ or (zicronapine or "lu 31 130" or "lu 31-130" or "lu31 130" or "lu31-130").mp.

168 zoloperone/ or (zoloperone or "lr 511" or lr511).mp.

169 zuclopenthixol/ or zuclopenthixol acetate/ or zuclopenthixol decanoate/ or (zuclopenthixol or clopenthixol or cisordinol or sedanaxol or zuclopenthixol or clopixol).mp.

170 clonidine/ or (adesipress or arkamin or atensina or caprysin or catapres or catapresan or catasan or chlofazolin or chlophazolin or chlophelin or clonidine or clofelin or clofeline or clomidine or clondine or clonicef or clonidin or clonidine or clonipresan or clonistada or clonnirit or clophelin or clopheline or daipres or dcpi or dichlorophenylaminoimidazoline or dixarit or duraclon or haemiton or hemiton or hypodine or isoglacon or jenloga or kapvay or "m 5041t" or melzin or normopresan or normopresin or paracefan or "st 155" or sulmidine or taitecin or "tenso timelet").mp.

171 Dexamethasone/ or (millicorten or maxidex or dexamethasone or dexpak or dexasone or oradexon or hexadecadrol or hexadrol or methylfluorprednisolone or decamet).mp.

176 lorazepam/ or (lorazepam or idalprem or sinestron or ativan or sedicepan or duralozam or orfidal or somagerol or apolorazepam or novolorazem or laubeel or donix or wy4036 or "wy 4036" or "wy-4036" or temesta or nuloraz or tolid).mp.

172 midazolam/ or (midazolam or "ro 21-3981" or "ro 21 3981" or versed or "ro 213981" or dormicum).mp.

173 diazepam/ or (diazemuls or apaurin or seduxen or faustan or sibazon or valium or stesolid or relanium).mp.

174 donepezil/ or (donepezil or aricept or aricept or asenta or "e 2020" or "e2020" or eranz or memac or memorit).mp.

175 rivastigmine/ or (rivastigmine or "ena 713" or ena713 or exelon or nimvastid or prometax or rivastigmin or "sdz 212 713" or "sdz 212-713" or "sdz 212713" or "sdz ena 713" or "sdz ena713" or "sdz212 713" or "sdz212-713" or sdz212713).mp.

176 or/1-176 [\*\*\*\*AntiPsychotic, benzodiazepines, cholinergic antagonists drugs - added\*\*\*\*]

177 confusion/ or acute confusion/ or restlessness/ or (Psychomotor\* adj2 Agitat\*).mp. or hallucination/ or auditory hallucination/ or hallucinosis/ or visual hallucination/ or illusion/ or visual illusion/ or delusion/ or paranoia/ or paranoid psychosis/ or (inattention or inattentive\*).ti,ab.

178 ("icu syndrome" or (intensive adj2 care adj2 unit adj2 syndrome)).ti,ab.

179 delirium/ or postoperative delirium/ or (delirious\* or delirium).ti,ab.

180 "disorders of higher cerebral function"/ or disorientation/ or organic brain syndrome/ or organic psychosyndrome/

181 (brain dysfunction/ and acute\*.ti,ab.) or ("acute brain dysfunction" or (acute adj2 brain adj2 dysfunction\*)) or "septic encephalopath\*").ti,ab.

182 brain disease/ and critically ill patient/

183 brain disease/ and exp sepsis/

184 ("acute brain failure" or "acute organic psychosyndrome\*" or "acute brain syndrome" or "metabolic encephalopath\*" or "acute psycho-organic syndrome\*" or "clouded state" or "clouding of consciousness" or "exogenous psychosis" or "toxi psychosis" or "icu psychosis").ti,ab.

185 brain disease/ and ((intensive adj2 care).mp. or hospital care/ or exp intensive care/ or "length of stay"/ or hospital admission/ or hospital discharge/ or hospital readmission/ or hospital utilization/ or hospitalization/ or patient transport/ or preoperative period/ or preoperative care/ or preoperative evaluation/ or preoperative treatment/)

186 or/177-185 [\*\*\*\*Confusion, delirium terms\*\*\*\*]

187 176 and 186 [\*\*\*\*Base clinical set\*\*\*\*]

188 (random\* or factorial\* or crossover\* or "cross over\*" or "cross-over\*" or placebo\* or (doubl\* adj blind\*) or (singl\* adj blind\*) or assign\* or allocat\* or volunteer\*).ti,ab.

189 crossover-procedure/ or double-blind procedure/ or randomized controlled trial/ or multicenter study/ or single-blind procedure/ or triple blind procedure/ or clinical trial.fs.

190 clinical trial or randomized controlled trial or controlled clinical trial or multicenter study).pt.

191 tu.fs.

192 or/188-191 [\*\*\*\*Cochrane Handbook EMBASE trial search strategy\*\*\*\*]

193 187 and 192 [\*\*\*\*Cochrane Handbook EMBASE trial search strategy\*\*\*\*]  
 194 limit 187 to (clinical trial or randomized controlled trial or controlled clinical trial or multicenter study)  
 195 or/193-194 [\*\*\*\*Final results limited to trials\*\*\*\*]

### Appendix 3. Cochrane Central Register of Controlled Trials Search Strategy

Database: Cochrane Central Register of Controlled Trials (July 20, 2017)

Search Strategy:

1 Antipsychotic drugs/ or Antipsychotic Agent/(antipsychotic\* or neuroleptic\* or (major adj2 (tranquilizer\* or tranquiliser\*))).mp.  
 2 aceperone/ or (aceperone or acetabutone or acetobutone or "r 3248" or r3248).mp.  
 3 Acepromazine/ or acepromazine maleate/ or (acepromazine or acetopromazine or vetranquil or acetylpromazine or acepromazine or calmivet or acetazine or notensil or plegicil or promace or soprintin or anatron or anergan or atravet or "cb 1522" or cb1522 or plegicin or plegicil or sedalin or soprontin).mp.  
 4 aceprometazine/ or (aceprometazine or acepromethazine or acetylpromethazine).mp.  
 5 acetophenazine / or (acetophenazine or acephenazine or "nsc 70600" or nsc70600 or "sch 6673" or sch6673 or tindal).mp.  
 6 adopraxine / or (adopraxine or adopraxin or "slv 313" or slv313).mp.  
 7 alimemazine/ or (alimemazin or alimemasine or alimemazin\* or alimezine or "bayer 1219" or electrotrimeprazine or methylpromazine or palpex or "rp 6549" or rp6549 or trimeprazine or trimeprezine or varialgil or nedeltran or panectyl or repeltin or temaril or temaryl or teralen or teralene or theralen or theralene or valergan or vallergeran).mp.  
 8 "alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol"/ or ("bms 181100" or bms181100 or "bmy 14802" or "bmy 14802 1" or "bmy 14802-1" or bmy14802 or "bmy14802 1" or "bmy14802-1" or bmy148021).mp.  
 9 "alpha [1 [2 (1,4 benzodioxan 5 yloxy)ethyl] 3 pyrrolidinyl] 4 fluoroacetophenone"/ or ("s 16924" or s16924).mp.  
 10 amitriptyline plus perphenazine/ or amitriptyline perphenazine/ or (amitriptyline or ((amitriptyline adj2 perphenazine) or "anxipress-d" or "duo-vil 2-10" or "duo-vil 2-25" or "duo-vil 4-10" or etrafon or etraphon or longopax or mutabon or mutanxion or mutaspline or "neuragon-a" or "neuragon-b" or peritriptyl or polybon or triavil or triptafen)).mp.  
 11 aplindore/ or (aplandore or "dab 452" or dab452 or palindore or "way dab 452" or " way dab452").mp.)  
 12 atypical antipsychotic agent/ or "1 cyclopropylmethyl 4 [2 (4 fluorophenyl) 2 oxoethyl]piperidine"/ or "1,2,3,4,8,9,10,10a octahydro 7bh cyclopenta[b][1,4]diazepino[6,7,1 hi]indole"/ or "2 amino n [4 [4 (1,2 benzisothiazol 3 yl) 1 piperazinyl]butyl]benzamide"/ or "2 chloro 11 (3 dimethylaminopropylidene)morphanthridine"/ or "4 (4 fluorophenyl) 1,2,3,6 tetrahydro 1 [4 (1,2,4 triazol 1 yl)butyl]pyridine"/ or "4,9 dibromo 6 (4 methyl 1 piperazinyl)benzo[b]pyrrolo[3,2,1 jk][1,4]benzodiazepine"/ or "7 [3 [4 (2,3 dimethylphenyl) 1 piperazinyl]propoxy] 2(1h) quinolinone"/ or "7 chloro 2 [[1 (2 methoxyphenyl) 4 piperidyl]methylaminomethyl] 1,4 benzodioxan"/ or "8 fluoro 4 [3 (2 methoxyethyl) 4 methyl 1 piperazinyl] 2 methyl 10h thieno[2,3 b][1,5]benzodiazepine"/ or atypical antipsychotic agent/ or (atypical adj2 (antipsychotic\* or neuroleptic\*)).mp. or abaperidone/ or (abaperidone or "fi 8602" or fi8602).mp. or alentamol/ or (alentamol or alentemol or "u 66444b" or "u 68552b" or "u 68553b" or u66444b or u68552b or u68553b).mp. or amisulpride/ or (aminosultopride or amisulpride or amisulpridum or "dan 2163" or dan2163 or sertol or socian or solian).mp. or amperozide/ or (amperozide or "fg 5606" or fg5606).mp. or aripiprazole/ or (aripiprazole or abilify or abilitat or "opc 14597" or opc14597).mp. or asenapine/ or (asenapine or "org 5222" or org5222 or saphris or sycrest).mp. or batelapine/ or (batelapine or "cgs 13429" or cgs13429).mp. or belaperidone/ or (belaperidone or balaperidone or "lu 111995" or lu111995).mp. or bifeprunox/ or (bifeprunox or "du 127090" or du127090).mp. or elopiprazole/ or (emonapride/ or (emonapride or emirace or nemonapride or "ym 09151" or "ym 09151 02" or "ym 09151 2" or "ym 09151-02" or "ym 09151-2" or ym09151 or "ym09151 02" or "ym09151 2" or "ym09151-02" or "ym09151-2" or ym0915102 or ym091512).mp. or flumezapine/ or (flumezapine or "ly 120363" or ly120363).mp. or fluoxetine plus olanzapine/ or ((fluoxetine adj2 olanzapine) or symbyax).mp. or fluperlapine/ or (fluperlapine or "nb 106689" or nb106689).mp. or iloperidone/ or (iloperidone or fanapt or fanaptum or "hp 873" or hp873 or "ilo 522" or ilo522 or zomaril).mp. or lurasidone/ or (lurasidone or latuda or "mk 3756" or mk3756 or "sm 13496" or sm13496 or "smp 13496" or smp13496).mp. or melperone/ or (melperone or bunil or buronil or eunerpan or "fg 5111" or fg5111 or flubuperone or melperon or methylperone or metylperone or metylperonum).mp. or "n (2 chloro 6 methylergolin 8alpha yl)pivalamide"/ or ("sdz 208 912" or "sdz 208-912" or "sdz 208912" or "sdz 912" or "sdz hdc 912" or "sdz hdc912" or "sdz208 912" or "sdz208-912" or sdz208912 or sdz912).mp. or "n (2,6 dimethylergolin 8alpha yl)pivalamide"/ or ("sdz 208 911" or "sdz 208-911" or "sdz 208911" or "sdz 911" or "sdz hac 911" or "sdz hac911" or "sdz208 911" or "sdz208-911" or sdz208911 or sdz911).mp. or "n cyclohexyl 4 [4 (4 fluorophenyl) 4 oxobutyl] 1 piperazinecarboxamide"/ or ("fg 5803" or fg5803).mp. or norclozapine/ or (norclozapine or demethylclozapine or desmethylclozapine).mp. or ocaperidone/ or (ocaperidone or "r 79598" or r79598).mp. or olanzapine/ or (olanzapine or anzatric or "dopin tab" or "jolyon md" or lanopin or lanzac or "ly 170053" or ly170053 or meltolan or midax or olace or oladay or olan or olandus or olanex



or olansek or olapin or olazax or oleanz or olexar or oltal or olzap or onza or "ozapin md" or psychozap or relprev or zalasta or zelta or zydis or zypadhera or zyprex or zyprexa or zyprexav).mp. or paliperidone/ or (paliperidone or invega or "paliperidone palmitate" or "r 76477" or r76477 or "ro 76477" or "ro 92670" or ro76477 or ro92670 or xeplion).mp. or panamesine/ or (panamesine or "emd 57445" or emd57445).mp. or pentiapine/ or pentiapine maleate/ or (pentiapine or "cgs 10746" or cgs10746 or "cgs 10746b" or cgs10746b).mp. or perlapine/ or (perlapine or "aw 14'2333" or "aw 142333" or aw142333 or perlapin).mp. or perospirone/ or (perospirone or lullan or "sm 9018" or sm9018).mp. or pridopidine/ or (pridopidine or "acr 16" or acr16 or "asp 2314" or asp2314 or "fr 310826" or fr310826 or huntexil).mp. or quetiapine/ or (quetiapine or "ici 204636" or "ici 204646" or ici204636 or ici204646 or seroquel or socalm or tienapine).mp. or remoxipride/ or (remoxipride or "a 33547" or a33547 or "fla 731" or fla731 or roxiam).mp. or rilapine/ or rilapine.mp. or sertindole/ or (sertindole or "lu 23174" or lu23174 or "s 1991" or s1991 or serdolect or serlect).mp. or sulpiride/ or (sulpiride or abilit or aiglonyl or arminol or dobren or dogmatil or dogmatyl or dolmatil or eglonyl or equilid or "fk 880" or fk880 or isnamide or levobren or levopraid or levosulpiride or meresa or miradol or neogama or sulfiride or sulpivot or sulpyride or synedil or vipral).mp. or sultopride/ or (sultopride or barneil or barnotil or "ms 5024" or ms5024 or sulfopride).mp. or tenilapine/ or tenilapine.mp. or tiospirone/ or (tiospirone or "bmy 13859" or bmy13859 or "mj 13859" or "mj 13859 1" or "mj 13859-1" or mj13859 or "mj13859 1" or "mj13859-1" or mj138591 or tiaspirone).mp. or volinanserine/ or (volinanserine or "m 100907" or m100907 or "mdl 100151" or "mdl 100907" or mdl100151 or mdl100907).mp. or ziprasidone/ or (ziprasidone or "cp 88059" or "cp 88059 01" or "cp 88059 27" or "cp 88059-01" or "cp 88059-27" or "cp 8805901" or "cp 8805927" or cp88059 or "cp88059 01" or "cp88059 27" or "cp88059-01" or "cp88059-27" or cp8805901 or cp8805927 or geodon or zeldox or zeldrox or zipsydon).mp. or zotepine/ or (zotepine or lodopin or nipolept).mp.

13 Azaperone/ or (azaperone or "r-1929" or r1929 or sedaperone or stresnil).mp.)

14 Benperidol/ or (benperidol or anquil or benperidone or benzoperidol or benzperidol or benperidolneuraxpharm or "cb 8089" or cb8089 or frenactyl or frenactil or glanimon or "mcn jr 4584" or "mcn jr4584" or phenactil or "r 4584" or r4584).mp.

15 berupipam/ or (berupipam or "nnc 22 0010" or "nnc22 0010").mp.

16 bitopertin/ or (bitopertin or paliflutine or "r 1678" or r1678 or "rg 1678" or rg1678 or "ro 4917838" or ro4917838).mp.

17 blonanserine/ or (blonanserine or "ad 5423" or ad5423 or lonasen).mp.

18 brexpiprazole or (brexpiprazole or "opc 34712" or opc34712).mp.

19 brofoxine/ or (brofoxine or dimetabrone or "fi 6820" or fi6820).mp.

20 bromospiperone/ or (bromospiperone or bromospiroperidol).mp. (0)

21 bromperidol/ or bromperidol decanoate/ or (bromperidol or impromen or "r 11,333" or "r 11333" or "r11,333" or r11333 or tesoprel or "improven decanoate" or "r 46,541" or "r 46541" or "r46,541" or r46541).mp.

22 Butaclamol/ or Dibenzocycloheptenes/ or ("ay 23,028" or "ay 23028" or "ay23,028" or "ay-23028" or ay23028 or butaclamol).mp.

23 butaperazine/ or (butaperazine or "ahr 3000" or "bayer 1362" or butaperazinum or butyrylperazin or butyrylperazine or megalactil or randolectil or randolectyl or repoise or "riker 595" or tyrylen).mp.

24 carfenazine/ or (carfenazine or carfenazinum or carphenazine or "nsc 71755" or nsc71755 or procethazine or proketazine or "wy 2445" or wy2445).mp.

25 cariprazine/ or (cariprazine or "mp 214" or mp214 or "rgh 188" or rgh188).mp.

26 carpipramine/ or (carpipramine or carbadipimidine or defecton or defekton or prazinil or "pz 1511" or pz1511 or "rp 21679" or rp21679).mp.

27 carvotroline/ or (carvotroline or "wy 47791" or wy47791).mp.

28 centbutindole/ or centbutindole.mp.

29 chlorothiazide plus reserpine/ or (chlorothiazide or "diupres-250" or "diupres-500").mp.

30 chlorphenethazine/ or (chlorphenethazine or chlorfenethazine or elroquil or marophen).mp.

31 chlorproethazine/ or (chlorproethazine or neuriplege or "rp 4909" or rp4909).mp.

32 chlorpromazine/ or chlorpromazine plus dexamphetamine/ or chlorpromazine sulfoxide/ or (chlorpromazine or "2601 a" or "4560 r p" or aminosin or aminosine or aminazin or aminazine or ampliactil or ampticil or ancholactil or aspersinal or bellacina or cepezet or chlomazine or "chlor pz" or chloractil or chlorazine or chlorbromasin or chlorderazine or chlorderazin or chlormazine or chlorpromanyl or chlorpromazin or chlorpromed or clonazine or clordelazin or clorpromaz or clorpromazine or clozine or contomin or duncan or elmarin or esmino or fenactil or hibanil or hibernal or hibernal or "hl 3746" or "hl 5746" or klorproman or klorpromazin or klorpromex or laractyl or largactil or largactyl or matcine or megaphen or megatil or "ml 5746" or neomazine or neurazine or novomazina or phenathyl or plegomazin or plegomazine or proma or promacid or promactil or promapar or promazil or promexin or propaphen or propaphenin or prozil or prozin or psychazine or psynor or "rp 4560" or sanopron or "skf 2601 a" or solidon or sonazine or taroctil or taroctyl or "thor prom" or thorazene or thorazine or torazina or "vegetamin a" or "vegetamin b" or winsumin or wintamine or wintermin or zuledin or "thora-dex" or opromazine or secotil).mp.

33 Chlorprothixene/ or (chlorprothixene or chloprothixene or “chlor prothixene” or chloroprothixene or chlorprothixen or chlorprothixenechloride or chlorprotixen or chlorprotixene or chlothixen or “n 714” or “n 7714” or “ro 4 0403” or “ro 40403” or taractan or tarasan or traquilan or troxen or truxal or truxaleta or truxaletten).mp.

34 cinuperone/ (cinuperone or “hr 375” or hr375).mp.

35 clocapramine/ or (clocapramine or “y 4153” or y4153).mp.

36 cloflumide mesilate/ or (“cloflumide mesylate” or “vufb 15496” or vufb15496).mp.

37 clofluperol/ or (clofluperol or seperidol).mp.

38 clopenthixol/ or or THIOXANTHENES/ or TRANQUILIZING AGENTS/ or clopenthixol decanoate/ or (clopenthixol or “ay 62021” or ay62021 or chlorpenthixol or chlorperphenthixene or chlorperphenthixene or ciatyl or cisordinol or clopenthixol or cloxipol or “n 746” or n746 or “nsc 64087” or nsc64087 or sordinol or zuclopenthixol).mp.

39 clopimozide/ or (clopimozide or “r 29,764” or “r 29764” or “r29,764” or r29764).mp.

40 clonipazan/ or (clonipazan or “skf 69634” or skf69634).mp.

41 clonipramine/ or (clonipramine or cremin or mosapramine or “y 516” or y516).mp.

42 clotiapine/ or (clotiapine or clotiapin or clotiapiene or entumin or entumine or “hf 2159” or hf2159).mp.

43 cp 903397/ or (“cp 903397” or cp903397).mp.

44 cryptenamine plus reserpine/ or (cryptenamine or “unitensen-r”).mp.

45 Clozapine/ or Dibenzazepines/ or Piperazines/ or clozapine derivative/ or clozapine n oxide/ or (alemoxan or azaleptin or clopine or clopsine or clozapin\* or clozaril or denzapine or dorval o rdozapine or elcrit or fazaclo or “hf 1854” or hf1854 or lapenax or leponex or lozapin\* or sizopin or versacloz or “wander compound” or zapen or zaponex).mp.

46 cyamemazine/ or (cyamemazine or cianatil or cyamepromazine or “fi 6229” or fi6229 or kyamepromazin or “rp 7204” or rp7204 or tercián).mp.

47 dexamphetamine plus prochlorperazine/ or ((dextroamphetamine adj2 sulfate adj2 prochlorperazine) or “eskatrol spansule”).mp.

48 dexamphetamine plus reserpine/ or ((dexamphetamine or dexserpine or dextroamphetamine) adj2 reserpine).mp.

49 diethylstilbestrol plus methyltestosterone plus reserpine/ or ((diethylstilbestrol adj2 methyltestosterone) or tylandril).mp.

50 dimetotiazine/ or (dimetotiazine or banistyl or dimethiotiazine or dimethiothazine or dimethothiazine or dimethotiazine ro dime-tiotiazine or fonazine or “il 6302”).mp.

51 dimevamide plus phenobarbital plus reserpine/ or ((dimevamide adj2 phenobarbital) or “neuro-centrine tablet\*”).mp.

52 dixyrazine/ or (dixyrazine or dixirazine or dixyrazin or dyxirazine or esocalm or esucos or metronal or roscal or “ucb 3412” or ucb3412).mp.

53 dolasetron mesilate/ or (dolasetron or anemet or anzemet or “mdl 73147” or “mdl 73147ef” or mdl73147 or mdl73147ef or zamanon).mp.

54 Droperidol/ or or droperidol plus fentanyl/ or droperidol plus fentanyl citrate/ or (droperidol or dehidrobenzoperidol or dehydrobenzoperidol or dehydrobenzoperiol or dehydrobenzperidol or dehydrobenzperidolum or dridol or droleptan or droperol or halkan or inaprine or inapsin or inapsine or “mcn jr 4749” or “mcn r 4749” or oridol or “r 4749” or sintodian or troperidol or xomolix or innovan or innovar or inoval or inovar or talamonal or thalamonal or disifelit).mp.

55 duoperone/ or (duoperone or “ahr 6646” or ahr6646).mp.

56 ephedrine sulfate plus reserpine/ or ((ephedrine adj2 sulfate) or renir).mp.

57 ethinylestradiol plus reserpine/ or ((ethinylestradiol adj2 reserpine) or estrosed or sergynol).mp.

58 etymemazine/ or (etymemazine or diquel or ethotrimiprazine or ethylisobutrazine or ethymemazine or nualt or “rp 6484” or rp6484 or sergetyl).mp.

59 Etazolate/ or Pyridines/ or (etazolate or sq20009 or “sq-20009” or “sq 20009”).mp.

60 farampator/ or (farampator or “cx 691” or cx691 or “org 24448” or org24448).mp.

61 fluanisone/ or (fluanisone or “anti pica” or antipica or fluanison\* or fluanizone or fluoanisone or haloanison or haloanisone or “md 2028” or md2028 or “r 2028” or “r 2167” or r2028 or r2167 or sedalande or sedalanide or solusediv).mp.

62 Flupenthixol/ or flupentixol decanoate/ or (flupentixol or flupenthixol\* or emergil or fluanxol or fluxanxol or “lc 44” or lc44 or “n 7009” or n7009 or siplaryl or siplarol or depixol or depot or “lu 5 110” or “lu 5110” or viscoleo).mp.

63 Fluphenazine/ or fluphenazine decanoate/ or fluphenazine enanthate/ or (fluphenazin\* or anatensil or anatensol or antasol or cenilene or dapotum or elinol or flufenan or flufenazine or flumezin or fluorfenazine or fluphenacin or “fluzine-p” or ftorphenazine or “luogen depot” or lyogen or lyorodin or moditen or moditin or omca or pacinol or permitil or phthorphenazine or potensone or prolisan or prolixene or prolixin\* or “s 94” or sevinol or sevinol or squaline or squalon\* or siquoline or “sq 4918” or sq4918 or tensofin or trancin or valamina or vespazin\* or “dapatum d25” or dapotum or decafen or flucan or fludecasine or fludecate or lyogen or mirenil or modocate or phlufdek or sydepres or flunanthate).mp.

64 Fluspirilene/ or (fluspirilene or fluspi or fluspirilen or imap or "mcn jr 6218" or "mcn jr6218" or "r 6218" or r6218 or redeptin or spirodifflamine or kivat).mp.

65 flutroline/ or (flutroline or "cp 36,584" or "cp 36584" or "cp36,584" or cp36584).mp.

66 "gamma endorphin[deenkaphalin]" or ((endorphin adj2 deenkaphalin) or "beta endorphin[6-17]" or "beta lipotropin[66-77]" or "org 5878" or org5878).mp.

67 gevetroline/ or (gevetroline or "wy 47384" or wy47384).mp.

68 glyceryl trinitrate plus pentaerythrityl tetranitrate plus reserpine/ or penite.mp.

69 Haloperidol/ or haloperidol decanoate/ or (haloperidol or alased or aloperidin\* or avant or binison or brotopon or celenase or cereen or cerenace or cizoren or depidol or dores or dozic or duraperidol or "einalon s" or fortunian or govotil or haldol or halidol or "halo-p" or halojust or halomed or haloneural or haloper or haloperil or haloperin or haloperitol or halopidol or halopol or halosten or haricon or "haridol-d" or keselan or linton or "lodomer-2" or "mcn jr 1625" or "mcn jr1625" or mixidol or novoperidol or "nsc 170973" or nsc170973 or peluces or perida or peridol or peridor or "r 1625" or r1625 or selezyme or seranace or serenase or serenelfi or siegoperidol or sigaperidol or transcodol or pericate or "r 13,672" or "r 13672" or senorm).mp.

70 hexamethonium chloride plus reserpine/ or (hexamethonium or reserthonium).mp.

71 hydralazine plus reserpine/ or hydrochlorothiazide plus potassium chloride plus reserpine/ or hydrochlorothiazide plus reserpine/ or (dralserp or (hydralazine adj2 reserpine) or "serpasil-apresoline" or "hydropresor dichlotride s" or "h.r.-50" or "hydro-reserp" or hydrochlorothiazide or hydroserpine or "medeserpine co" or "serpasil-esidrix").mp.

72 hydrochlorothiazide plus reserpine plus secbutabarbital/ or ((hydrochlorothiazide adj2 reserpine adj2 secbutabarbital) or butiserpazide).mp.

73 hydroflumethiazide plus potassium chloride plus reserpine/ or ((hydroflumethiazide adj4 reserpine) or rautrax).mp.

74 hydroflumethiazide plus reserpine/ or ((hydroflumethiazide adj2 reserpine) or salutensin\*).mp.

75 isofloxythepin/ or (isofloxythepin or "vufb 10662").mp.

76 isomolpan/ or (isomolpan or "cgs 15855" or "cgs 15855 a" or "cgs 15855a" or cgs15855 or cgs15855a).mp.

77 isopropamide iodide plus prochlorperazine maleate/ or ((isopropamide adj4 prochlorperazine) or "combid spansule").mp.

78 lenperone/ or (lenperone or "ahr 2277" or ahr2277 or elanone).mp.

79 levomepromazine/ or (levomepromazine or "apo-methoprazine" or "bayer 1213" or "cl 36467" or "cl 39743" or cl36467 or cl39743 or hirnamin or mepromazine or levium or promazine or levomeprazine or levopromazin\* or levoprome or levozin or mepromazine or methotrimprazine or methozane or milezin or minozinan or neozine or neuractil or neurocil or nirvan or nozinan or "rp 7044" or rp7044 or sinogan or "sk and f 5116" or "skf 5116" or skf5116 or tiscerin or tiscrin or veractil).mp.

80 lithium/ or lithium.mp.

81 Loxapine/ or loxapine succinate/ or (loxapine or adasuve or "alxz 004" or alxz004 or "az 004" or az004 or "cl 62,362" or "cl 62362" or "cl62,362" or cl62362 or "cl 71563" or "cl-71563" or cl71563 or loxapinsuccinate or clozapexin\* or loxapane or loxapin\* or loxitane or oxilapine or "sum 3170" or sum3170 or daxolin or desconex or loxapac).mp.

82 maroxepine/ or maroxepine.mp.

83 mazapertine/ or (mazapertine or "rwj 37796" or rwj37796).mp.

84 mepiprazole/ or meprobamate plus promazine/ or (mepiprazole or "emd 16923" or emd16923 or psigodal or prozine or meprobamate).mp.

85 Mesoridazine/ or Phenothiazines/ or Tranquilizing Agents/ or mesoridazine besylate/ or (mesoridazin\* or esoridazine or lidanar or lidanil or mesorin or "nc 123" or (thioridazine adj2 sulfoxide) or "tps 23" or serentil).mp.

86 methamphetamine plus reserpine/ or ((methamphetamine adj2 reserpine) or "du-oria").mp.

87 Methiothepin/ or Dibenzothiepins/ or Piperazines/ or methyclothiazide plus reserpine/ or (methiothepin\* or metitepine).mp.

88 methopromazine/ or (methopromazine or methoxypropazine or metopromazine or "diutensen-r").mp.

89 Methotrimprazine/ or (levopromazine or tizercine or methotrimprazine or levomepromazine or levomeprazin or tiscrin or tizertsin).mp.

90 metofenazate/ or (metofenazate or frenolon or metaphenazine or methophenazine or metophenazine or phrenolon).mp.

91 Molindone/ or indoles/ or (molindon\* or "en 1733a" or en1733a or lidone or moban or molindor).mp.

92 moperone/ or (moperone or luvaren or luvarena or "methyl peridol" or methylperidol\* or moperon or "r 1658").mp.

93 "n [(1 butyl 2 pyrrolidinyl)methyl] 2,3 dihydro 2 methyl 5 sulfamoyl 7 benzofurancarboxamide"/ or ("y 20024" or y20024).mp.

94 "n [3 (4 fluorophenyl) 3 (4 phenylphenoxy)propyl]sarcosine"/ or ("alx 5407" or alx5407 or NFPS).mp.

95 "n [4 [2 (6 cyano 1,2,3,4 tetrahydro 2 isoquinolinyl)ethyl]cyclohexyl] 4 quinolinecarboxamide"/ or ("sb 277011" or "sb 277011a" or sb277011 or sb277011a).mp.

96 neboglamine/ or (neboglamine or "cr 2249" or cr2249 or "xy 2401" or xy2401).mp.

97 nicotinic acid plus pentetrazole plus reserpine/ or ((nicotinic adj4 pentetrazole adj4 reserpine) or (nicozol adj2 reserpine)).mp.

98 noctran/ or noctran.mp.

99 norchlorpromazine/ or (norchlorpromazine or demethylchlorpromazine or demonomethylchlorpromazine or desmethylchlorpromazine or desmonomethylchlorpromazine or monodesmethylchlorpromazine).mp.

100 Ondansetron/ or Imidazoles/ or (ondansetron or gr38032f or "gr 38032f" or "sn 307" or sn307 or "gr-38032f" or "sn-307" or zofran).mp.

101 oxiperomide/ or (oxiperomide or "r 4714" or r4714).mp.

102 oxypertine/ or (oxypertin\* or "cl 77328" or cl77328 or equipertine or forit or opertil or oxipertin or oxypertin or "win 18501 2" or "win 18501-2" or "win 185012" or "win18501 2" or "win18501-2" or win185012).mp.

103 oxyprothepine/ or oxyprothepine decanoate/ or (oxyprothepine or oxyprothepin).mp.

104 pecazine/ or (pecazine or lacumin or mepasin or mepazine or nothiazine or "p 391" or pacatal or pacatol or pactal or papital or paxital or pecazine or "w 1224").mp.

105 Penfluridol/ or (penfluridol or "mcn jr 16,341" or "mcn jr 16341" or micefal or "r 16,341" or "r 16341" or semap or "r 16341" or "r-16341" or r16341).mp.

106 Perazine/ or (perazine or taxilan).mp.

107 pentaerythrityl tetranitrate plus reserpine/ or pentaerythrityl tetranitrate plus reserpine plus secbutabarbitol/ or (pentaerythrityl or pentaserpine or respet or pentraline).mp.

108 pentobarbital plus reserpine/ or ("nambu-serpine" or (pentobarbital adj2 reserpine)).mp.

109 perazine/ or (perazine or "p 725" or pernazine or taxilan).mp.

110 periciazine/ or (periciazine or aolect or neulactil or neuleptil\* or periciazinum or pericyazine or propericiazine or propericiazin or propericiazine or "rp 8909" or "skf 20716").mp.

111 perimetazine/ or (perimetazine or "1317 an" or "an 1317" or an1317 or lepryl or perimethazine).mp.

112 Perphenazine/ or perphenazine decanoate/ or perphenazine enanthate.mp. or (perphenazine or chlorperphenazine or chlorpiprazine or chlorpiprozone or decentan or etaperazine or ethaperazine or "f-mon" or fentazin or leptopsique or peratsin or perfenazine or perferazine or pernamed or perphenan or perphenazin\* or "perzine-p" or porazine or "sch 3940" or thilatazin or tranquisan or trifalon or trilafan or trilafon or trilifan or triliphan or triomin).mp.

113 ("pf 217830" or pf217830 or "pf 2400013" or pf2400013 or "pf 3463275" or pf3463275).mp.

114 phenobarbital plus reserpine/ or phenobarbital plus reserpine plus theobromine/ or phenobarbital plus reserpine plus thiamine.mp. or ((phenobarbital adj2 reserpine) or "solfo-serpine" or bromoserpin or "theo-serp" or "theobarb-r" or theoserpin or besertal or "neo-slowten").mp.

115 picobenzide/ or (picobenzide or dosetil or "m 14012 4" or "ma 14012" or picobenzamide).mp.

116 piflutixol/ or piflutixol.mp.

117 pimavanserine/ or (pimavanserine or "acp 103" or acp103).mp.

118 pimethixene/ or (pimethixene or "bp 400" or "bp 400 e" or "bp 400e" or bp400 or bp400e or muricalm or pimetixin).mp.

119 Pimozide/ or (pimozide or antalon or "mcn jr 6238" or opiran or orap or pimocide or pimoride or pinozide or pizide or "r 6238" or r6238).mp.

120 pipamperone/ or (pipamperone or dipeperon or dipiperon or "dl piperonyl" or floropipamide or "piperonyl of pripamperone of r 3345" or r3345).mp.

121 piperacetazine/ or (piperacetazine or "pc 1421 or pc1421" or guide).mp.

122 pipotiazine/ or pipotiazine palmitate/ or pipotiazine undecenoate/ or (pipotiazine or "9366 rp" or piportil or pipothiazine or "rp 19366" or rp19366 or "il 19552" or il19552 or "rp 19552" or rp19552 or rp 19551).mp.

123 pirenperone/ or polythiazide plus reserpine/ or (pirenperone or "r 47,465" or "r 47465" or "r 50656" or "r47,465" or r47465 or r50656 or "renese r" or "renese-r").mp.

124 pomaglumetad methionil/ or ("pomaglumetad methionil" or "ly 2140023" or ly2140023).mp.

125 Prochlorperazine/ or prochlorperazine edisylate/ or prochlorperazine maleate/ or (compazine or prochlorperazine or "6140 rp" or antinaus or "bayer a 173" or "bayer 173" or capazine or chlormepazine or chlorpeazine or chlorperazine or compro or dicopal or emelent or klometil or kronocin or meterazine or metherazine or nautisol or nipodal or normalmin or pasotomin or prochlor or prochlorpemazine or prochlorperacine or prochlorperzine or prochlorpromazine or prochlorperazine or procot or "rp 6140 ir rp6140" or "sk and f 4657" or "skf 4657" or skf4657 or temetil or temetil or buccastem or dhaperazine or emeteral or emetiral or nibromin or proclozine or procomp or stemetil or stemzine).mp.

126 profenamine/ or (profenamine or dibutil or ethopropazine or etopropazine or isothazine or isothiazine or lysivane or parcidol or pardisol or parfezin\* or parkisol or parphezin or parsidol or parsitan or phenopropazine or "profenamine hydrochloride" or prophenamine or rochipel or rodipal or "rp 3356" or "sc 2538").mp.

- 127 Promazine/ or (promazine or alofen or alophen or ampazine or amprazim or centractyl or delazin or esparin or lete or liranol or "neo hibernex" or neuroplegil or piarine or prazine or "pro tan" or promantine or promanyl or promilene or promwill or protactil or protactyl or romthiazine or romtiazin or "rp 3276" or sediston or sinophenin\* or sparine or tomil or varophen or verophen or "wy 1094").mp.
- 128 propantheline bromide plus thiopropazate/ or ((propantheline adj4 thiopropazate) or "pro-banthine").mp.
- 129 propiomazine/ or propiomazine maleate/ or (propiomazine or "cb 1678" or cb1678 or largon or propionylpromethazine or propriomazine or propromazine or dorevane or indorm or phenoctyl or propavan or "wy 1359").mp.
- 130 propionylpromazine/ or (propionylpromazine or combelen or dipropiomazine or propiopromazine or tranvet).mp.
- 131 prothipendyl/ or (prothipendyl or "ay 5603" or ay5603 or azacon or "d 206" or d206 or dominal or inalforte or largophren or "lg 206" or lg206 or phrenotropin or prothipendil or protipendil or protipendyl or timovan or tolnate or tumovan).mp.
- 132 protoveratrine A plus protoveratrine B plus reserpine/ or protoveratrine A plus reserpine/ or pyrrobutamine plus reserpine/ or (protoveratrine or "veralba r" or verapene or "protalba-r" or pyrrobutamine or (sandril adj2 pyronil)).mp.
- 133 quinethazone plus reserpine/ (quinethazone or hydromax).mp.
- 134 Raclopride/ or raclopride tartrate/ or (raclopride or "flb-472" or "flb 472" or "fla-870" or "fla 870" or flb472 or fla870 or "a 40664" or a40664).mp.
- 135 Remoxipride/ or REMOXIPRIDE (nm) or (remoxipride or fla731 or "fla-731").mp.
- 136 Reserpine/ or reserpine plus secbutabarbitol/ or reserpine plus trichlormethiazide/ or (reserpine or abten or alkarau or alserin or anquil or apoplon\* or austrapine or boiserpine or crystoserpin or crystoserpine or elserpine or eroseprin or eskaserp or evraloid or hiserpia or hypersine or koglucoïd or lemiserp or maviserpine or "neo antitensol" or quiescin or "r-e-s" or "rau sed" or "rau-sed" or raudixoid or rauloydin or raunervil or raupina or raurine or roused or rousedan or rousedyl or rauserpine or rausingle or rautensin or rauwilid or rauwiloid or rauwolfaf or repoid or resercen or reserpamed or reserpen or reserpene or reserpex or reserpil or reserpin or reserpoid or resine or riserpa or rivasin or roxel or roxinoid or sandril or sedaraupin or serfin or serfolia or serolfia or serpalan or serpanray or serpasil or serpasol or serpate or serpen or serpena or serpentina or serpiloid or serpine or serpvite or sertabs or sertensin or sertina or "vio serpine" or "vio-serpine" or "v serp" or butiserpine or metatensin or naquival).mp.
- 137 rimcazole/ or (rimcazole or "bw 234" or "bw 234u" or bw234 or bw234u).mp.
- 138 Risperidone/ or (risperidone or belivon or consta or neripros or noprenia or "r 64766" or r64766 or "r-64766" or riperidon or risolept or rispen or risperdal or rispid or rispolet or rizodal or sequinan or zargus or zofredal).mp.
- 139 Ritanserine/ or RITANSERIN (nm) or (ritanserine or "r-55667" or r55667 or "r 55667").mp.
- 140 romergoline/ or (romergoline or "fce 23884" or fce23884 or "ls 111871" or ls111871).mp.
- 141 savoxepine/ or (savoxepine or "cgp 19486" or "cgp 19486a" or cgp19486 or cgp19486a or cipazoxapine or savoxapine).mp.
- 142 ("sb 773812" or sb773812).mp.
- 143 seridopidine/ or (seridopidine or "acr 343" or acr343).mp.
- 144 setoperone/ or (setoperone or "r 52,245" or r 52245).mp.
- 145 Spiperone/ or Butyrophenones/ or Spiro Compounds/ or (spiperone or "r 5147" or r5147 or spiroperidol or spiroptan).mp.
- 146 sulfuridazine/ or (sulfuridazine or inofal or "tpn 12").mp.
- 147 Sulpiride/ or (sulpiride or tepavil or lebopride or "vertigo meresa" or pontiride or sulperide or ekilid or sulp or sulpor or "vertigo-meresa" or dolmatil or digton oe aiglonyl or guastil or sulpitol or meresa or synedil or deponerton or arminol or neogama or eglonyl or sulpivert or "vertigo-neogama" or desisulpid or psicocen or dogmatil or "vertigo neogama").mp.
- 148 tefludazine/ or (tefludazine or "lu 18 012" or "lu 18-012" or "lu 18012" or "lu18 012" or "lu18-012" or lu18012).mp. or tepirindole/ or (tepirindole or "hr 592" or hr592 or "ru 27592" or ru27592).mp.
- 149 thiopropazate/ or (thiopropazate or artalan or dartal or dartalan or dartan or "sc 7105" or thiopropazat).mp.
- 150 thioproperazine/ or thioproperazine methanesulfonate/ or (thioproperazine or "rp 7843" or thioperazine or majeptil or mayeptil or vontil).mp.
- 151 Thioridazine/ or (thioridazine or aldazine or apothioridazine or calmaril or mallorol or malloryl or meleril or mellaril or mellerets or mellerette\* or melleril or mellerzin or melleryl or melzine or mepiozin or orsanil or ridazin or ridazine or rideril or sonapax or thiomed or thioradazine or thioridacine or thioridazide or thioridazin or thioridazine or thioril or thiosia or thoridazine or thiozine or thioridazineneurazpharm or tioridazin or tioridazine or "tp 21" or tpzl).mp.
- 152 Thiothixene/ or tiotixene/ or (tiotixene or cis thiothixene or "cp 12,252 1" or "cp 12252 1" or "cp 122521" or "cp12,252 1" or cp12252 1 or cp122521 or navan or navane or "nsc 108165" or nsc108165 or onaven or orbinamon or "p 4657 b" or "p 4657b" or p4657b or thiotixene or thiotixin or thiotixine or thixit).mp.
- 153 Tiapride Hydrochloride/ or Tiapride/ or (tiapride or delpral or "flo 1347" or "flo-1347" or flo1347 or italprid or sereprile or thiapride or tiapridal or tiapridex or tiaprizal or equilibrium).mp.
- 154 timiperone/ or (timiperone or "dd 3480" or dd3480 or tolopelon).mp.

- 155 tranlycypromine plus trifluoperazine/ or ((tranlycypromine adj2 trifluoperazine) or jatrosom or parstelin or stelapar).mp.
- 156 triethylperazine/ or triethylperazin\*.mp.
- 157 Trifluoperazine/ or trifluoperazine derivative/ or (trifluoperazine or apotrifluoperazine or calmazine or eskazine or eskaziny/ or espazine or fluoperazine or flupazine or fluperin or flurazin or "iremo-pierol" or jatroneural or leptazine or modalina or modiur or nerolet or nylipton or operzine or oxyperazine or psyrazine or "sk and f 5019" or "skf 5019" or sporalon or stelazine or terfluzin\* or triflumed or trifluoperazide or trifluoperzine or trifluperazine or trifluoroperazine or trifluorperacine or trifluorperazine or trifluperazine or triflurin or triftazin or triftazine or triftazinum or trincalm or triozone or triptazine or triphthasine or triphthazine).mp.
- 158 Trifluoperidol/ or (trifluoperidol or "mcn jr 2498" or psicoperidol or "r 2498" or r2498 or trifluoperidol or triperidol or trisedyl or trisedil).mp.
- 159 Triflupromazine/ or (triflupromazine or adazine or fluopromazin or fluopromazine or fluorofen or "mc 4703" or mc4703 or nivoman or psyquil or siquil or "skf 4648 a" or "skf 4648a" or skf4648a or trifluopromazine or vespral or vesprin or vetame).mp.
- 160 umespirone/ or (umespirone or "kc 7218" or "kc 9172" or kc7218 or kc9172).mp.
- 161 vabicaserin/ or (vabicaserin or "sca 136" or sca136).mp.
- 162 zetidoline/ or (zetidoline or "dl 308" or "dl 308 it" or "dl 308it" or dl308 or dl308it).mp.
- 163 zicronapine/ or (zicronapine or "lu 31 130" or "lu 31-130" or "lu31 130" or "lu31-130").mp.
- 164 zoloperone/ or (zoloperone or "lr 511" or lr511).mp.
- 165 zuclopenthixol/ or zuclopenthixol acetate/ or zuclopenthixol decanoate/ or (zuclopenthixol or clopenthixol or cisordinol or sedanol or zuclopenthixol or clopixol).mp.
- 166 clonidine/ or (adesipress or arkamin or atensina or caprysin or catapres or catapresan or catasan or chlofazolin or chlophazolin or chlophelin or clonidine or clofelin or clofeline or clomidine or clondine or clonice/ or clonidin or clonidine or clonipresan or clonistada or clonnirit or clophelin or clopheline or daipres or dc/ai or dichlorophenylaminoimidazoline or dixerit or duraclon or haemiton or hemiton or hypodine or isoglauc/ or jenloga or kapvay or "m 5041t" or melzin or normopresan or normopresin or paracefan or "st 155" or sulmidine or taitecin or "tenso timelet").mp.
- 167 Dexamethasone/ or (millicorten or maxidex or dexamethasone or dexpak or dexasone or oradexon or hexadecadrol or hexadrol or methylfluorprednisolone or decamet).mp.
- 168 lorazepam/ or (lorazepam or idalprem or sinestron or ativan or sedicepan or duralozam or orfidal or somagerol or apolorazepam or novolorazem or laubeel or donix or wy4036 or "wy 4036" or "wy-4036" or temesta or nuloraz or tolid).mp.
- 169 midazolam/ or (midazolam or "ro 21-3981" or "ro 21 3981" or versed or "ro 213981" or dormicum).mp.
- 170 diazepam/ or (diazemuls or apaurin or seduxen or faustan or sibazon or valium or stesolid or relanium).mp.
- 171 donepezil/ or (donepezil or aricept or aricept or asenta or "e 2020" or "e2020" or eranz or memac or memorit).mp.
- 172 rivastigmine/ or (rivastigmine or "ena 713" or ena713 or exelon or nimvastid or prometax or rivastigmin or "sdz 212 713" or "sdz 212-713" or "sdz 212713" or "sdz ena 713" or "sdz ena713" or "sdz212 713" or "sdz212-713" or sdz212713).mp.
- 173 or/1-172 [\*\*\*\*AntiPsychotic, benzodiazepines, cholinergic antagonists drugs - added\*\*\*\*]
- 174 Confusion/ or Psychomotor Agitation/ or hallucinations/ or illusions/ or delusions/ or paranoid behavior/ or acute confusion/ or restlessness/ or (Psychomotor\* adj2 Agitat\*).mp. or hallucination/ or auditory hallucination/ or hallucinosis/ or visual hallucination/ or illusion/ or visual illusion/ or delusion/ or paranoia/ or paranoid psychosis/ or (inattention or inattentive\*).ti,ab.
- 175 ("icu syndrome" or (intensive adj2 care adj2 unit adj2 syndrome)).ti,ab.
- 176 delirium, dementia, amnesic, cognitive disorders/ or psychotic disorders/ or delirium/ postoperative delirium/ or (delirious\* or delirium).ti,ab. Or "disorders of higher cerebral function"/ or disorientation/ or organic brain syndrome/ or organic psychosyndrome/
- 177 (brain dysfunction/ and acute\*.ti,ab.) or ("acute brain dysfunction" or (acute adj2 brain adj2 dysfunction\*) or "septic encephalopath").ti,ab.
- 178 (brain diseases/ and critical illness/) or brain disease/ and critically ill patient/
- 179 (brain diseases/ and sepsis/) or (brain disease/ and exp sepsis/ )
- 180 ("acute brain failure" or "acute organic psychosyndrome\*" or "acute brain syndrome" or "metabolic encephalopath\*" or "acute psycho-organic syndrome\*" or "clouded state" or "clouding of consciousness" or "exogenous psychosis" or "toxi psychosis" or "icu psychosis").ti,ab.
- 181 )brain diseases/ and (critical illness/ or Intensive Care/ or critical care/ or hospitalization/ or "length of stay"/ or patient admission/ or patient discharge/ or patient readmission/ or patient transfer/ or preoperative care/)) or (brain disease/ and ((intensive adj2 care).mp. or hospital care/ or exp intensive care/ or "length of stay"/ or hospital admission/ or hospital discharge/ or hospital readmission/ or hospital utilization/ or hospitalization/ or patient transport/ or preoperative period/ or preoperative care/ or preoperative evaluation/ or preoperative treatment/))
- 182 or/174-181 [\*\*\*\*Confusion, delirium terms\*\*\*\*]
- 183 173 and 182 [\*\*\*\*Base clinical set\*\*\*\*]

## Appendix 4. EBSCO - Cumulative Index to Nursing and Allied Health Literature Search Strategy

Database: EBSCO - Cumulative Index to Nursing and Allied Health Literature (1982 to July 20, 2017)

Search Strategy:

S1 (TX dolasetron OR anemet OR anzemet OR “mdl 73147” OR “mdl 73147ef” OR mdl73147 OR mdl73147ef OR zamanon OR droperidol OR dehidrobenzoperidol OR dehydrobenzoperidol OR dehydrobenzoperiol OR dehydrobenzperidol OR dehydrobenzperidolum OR dridol OR droleptan OR droperol OR halkan OR inaprine OR inapsin OR inapsine OR “mcn jr 4749” OR “mcn r 4749” OR ORidol OR “r 4749” OR sintodian OR troperidol OR xomolix OR innovan OR innovar OR inoval OR inovar OR talamonal OR thalamonal OR disifelit OR duoperone OR “ahr 6646” OR ahr6646 OR (ephedrine N2 sulfate) OR renir OR Estrosed OR sergynol OR etymemazine OR diquel OR ethotrimprazine OR ethylisobutrazine OR ethymemazine OR nital OR “rp 6484” OR rp6484 OR sergetyl OR etazolate OR sq20009 OR “sq-20009” OR “sq 20009” OR Farampat OR OR “cx 691” OR cx691 OR “ORg 24448” OR ORg24448 OR fluanisone OR “anti pica” OR antipica OR fluanison\* OR fluanizone OR fluoanisone OR haloanison OR haloanisone OR “md 2028” OR md2028 OR “r 2028” OR “r 2167” OR r2028 OR r2167 OR sedalande OR sedalanide OR solusediv)

S2 (TX flupentixol OR flupenthixol\* OR emergil OR fluanxol OR fluxanxol OR sipliril OR siplarol OR depixol OR viscoleo OR fluphenazin\* OR anatensil OR anatensol OR antasol OR cenilene OR dapotum OR elinol OR flufenan OR flufenazine OR flumezin OR fluORfenazine OR fluphenacin OR “fluzine-p” OR ftORphenazine OR lyogen OR lyORodin OR moditen OR moditin OR omca OR pacinol OR permitil OR phthORphenazine OR potensone OR prolixan OR prolixene OR prolixin\* OR “s 94” OR sevinol OR sevinol OR squaline OR squalon\* OR siquoline OR sq4918 OR tensofin OR trancin OR valamina OR vespazin\* OR “dapatum d25” OR dapotum OR decafen OR flucan OR fludecaine OR fludecate OR lyogen OR mirenil OR moderate OR phlufdek OR sydespre OR flunanthate OR fluspirilene OR fluspi OR fluspirilen OR imap OR r6218 OR redeptin)

S3 (TX spirodiflamine OR kivat OR Flutroline OR “cp 36584” OR “cp36,584” OR cp36584 OR “org 5878” OR org5878 OR gevetroline OR “wy 47384” OR wy47384 OR penite OR haloperidol OR alased OR aloperidin\* OR avant OR binison OR brotopon OR celenase OR cereen OR cerenace OR cizORen OR depidol OR dozic OR duraperidol OR “einalon s” OR fORTunan OR govotil OR haldol OR halidol OR “halo-p” OR halojust OR halomed OR haloneural OR haloper OR haloperil OR haloperin OR haloperitol OR halopidol OR halopol OR halosten OR haricon OR “haridol-d” OR keselan OR linton OR “lodomer-2” OR “mcn jr 1625” OR “mcn jr1625” OR mixidol OR novoperidol OR “nsc 170973” OR nsc170973 OR peluces OR perida OR peridol OR peridOR OR “r 1625” OR r1625 OR selezyme OR seranace OR serenace OR serenase OR serenelfi OR siegoperidol OR sigaperidol OR trancodol OR pericate OR “r 13,672” OR “r 13672” OR senORm OR hexamethonium OR reserthonium OR dralserp OR (hydralazine N2 reserpine) OR “serpasil-apresoline” OR “hydropresOR dichloride s” OR “hydro-reserp” OR hydrochlORothiazide OR hydroserpine OR “medeserpine co” OR “serpasil-esidrix” OR butiserpazide OR rautraX OR salutensin\* OR isofloxythepin OR “vufb 10662” OR isomolpan OR “cgs 15855” OR “cgs 15855 a” OR “cgs 15855a” OR cgs15855 OR cgs15855a OR (isopropamide N4 prochlorperazine) OR “combid spansule” OR lenperone OR “ahr 2277” OR ahr2277 OR elanone OR levomepromazine OR “apo-methoprazine” OR “bayer 1213” OR “cl 36467” OR “cl 39743” OR cl36467 OR cl39743 OR hirnamin OR mepromazine OR levium OR promazine OR levomeprazine OR levopromazin\* OR levoprome OR levozin OR mepromazine OR methotrimprazine OR methozane OR milezin OR minozinan OR neozine OR neuractil OR neurocil OR nirvan OR nozinan OR “rp 7044” OR rp7044 OR sinogan OR “skf 5116” OR skf5116 OR tiscerin OR tiscerin OR veractil)

S4 (TX lithium OR loxapine OR adasuve OR “alz 004” OR alz004 OR “az 004” OR az004 OR “cl 62,362” OR “cl 62362” OR “cl62,362” OR cl62362 OR “cl 71563” OR “cl-71563” OR cl71563 OR loxapinsuccinate OR cloxazepin\* OR loxapane OR loxapin\* OR loxitane OR oxilapine OR “sum 3170” OR sum3170 OR daxolin OR desconex OR loxapac OR maroxepine OR mazapertine OR “rwj 37796” OR rwj37796 OR mepiprazole OR “emd 16923” OR emd16923 OR psigodal OR prozine OR meprobamate OR mesORidazin\* OR esORidazine OR lidanar OR lidanil OR mesORin OR “nc 123” OR (thiORidazine N2 sulfoxide) OR “tps 23” OR serentil OR (methamphetamine N2 reserpine) OR methiothepin\* OR metitepine OR methopromazine OR methoxypromazine OR metopromazine OR “diutensen-r” OR levopromazine OR tizercine OR methotrimprazine OR levomepromazine OR levomeprazin OR tiscerin OR tizertsin)

S5 (TX metofenazate OR frenolon OR metaphenazine OR methophenazine OR metophenazine OR phrenolon OR molindon\* OR “en 1733a” OR en1733a OR lidone OR moban OR molindOR OR moperone OR luvatren OR luvatrene OR “methyl peridol” OR methylperidol\* OR moperon OR “r 1658” OR “y 20024” OR y20024 OR “Alx 5407” OR alx5407 OR NFPS OR “sb 277011” OR “sb 277011a” OR sb277011 OR sb277011a OR neboglamine OR “cr 2249” OR cr2249 OR “xy 2401” OR xy2401 OR (nicotinic N4 pentetrazole N4 reserpine) OR (nicozol N2 reserpine) OR noctran OR ORchlORpromazine OR demethylchlORpromazine OR demonomethylchlORpromazine OR desmethylchlORpromazine OR desmonomethylchlORpromazine OR monodesmethylchlORpromazine OR ondansetron OR gr38032f OR “gr 38032f” OR “sn 307” OR sn307 OR “gr-38032f” OR “sn-307” OR zofran OR oxipromide OR “r 4714” OR r4714 OR oxypertin\* OR “cl 77328” OR cl77328 OR equipertine OR fORit OR opertil OR oxipertin

OR oxyperthin OR "win 18501 2" OR "win 18501-2" OR "win 185012" OR "win18501 2" OR "win18501-2" OR win185012 OR oxyprothepine OR oxyprothepin OR pecazine OR lacumin OR mepasin OR mepazine OR nothiazine OR "p 391" OR pacatal OR pacatol OR pactal OR papital OR paxital OR pecazine OR "w 1224" OR penfluridol OR "mcn jr 16341" OR micefal OR "r 16341" OR semap OR "r 16341" OR "r-16341" OR r16341 OR perazine OR taxilan)

S6 (TX pentaerythrityl OR pentaserpine OR respet OR pentraline OR "nambu-serpine" OR (pentobarbital N2 reserpine) OR perazine OR "p 725" OR pernazine OR taxilan OR pericazine OR aolept OR neulactil OR neuleptil\* OR periciazinum OR pericyazine OR propercazine OR propericiazin OR propericazine OR "rp 8909" OR "skf 20716" OR perimetazine OR "1317 an" OR "an 1317" OR an1317 OR lepryl OR perimethazine OR perphenazine OR chlORperphenazine OR chlORpiprazine OR chlORpiprozone OR decentan OR etaperazine OR ethaperazine OR "f-mon" OR fentazin OR leptopsique OR peratsin OR perfenazine OR perferazine OR pernamed OR perphenan OR perphenazin\* OR "perzine-p" OR pORazine OR "sch 3940" OR thilatazin OR tranquisan OR trifalon OR trilafan OR trilafon OR trilifan OR triliphan OR triomin OR "pf 217830" OR pf217830 OR "pf 2400013" OR pf2400013 OR "pf 3463275" OR pf3463275 OR (phenobarbital N2 reserpine) OR "solfo-serpine" OR bromoserpin OR "theo-serp" OR "theobarb-r" OR theoserpin OR besertal OR "neo-slowten" OR Picobenzide OR dosetil OR "m 14012 4" OR "ma 14012" OR picobenzamide OR piflutixol OR pimavanserin OR "acp 103" OR acp103 OR pimethixene OR "bp 400" OR "bp 400 e" OR "bp 400e" OR bp400 OR bp400e OR muricalm OR pimetixin OR pimozone OR antalon OR "mcn jr 6238" OR opiran OR ORap OR pimocide OR pimORide OR pinozone OR pizide OR "r 6238" OR r6238 OR pipamperone OR dipeperon OR dipiperon OR "dl piperonyl" OR flORopipamide OR "piperonyl of pripamperone of r 3345" OR r3345 OR piperacetazine OR "pc 1421OR pc1421" OR quide OR pipotiazine OR "9366 rp" OR pipORtil OR pipothiazine OR "rp 19366" OR rp19366 OR "il 19552" OR il19552 OR "rp 19552" OR rp19552 OR rp 19551 OR pirenperone OR "r 47465" OR "r 50656" OR r47465 OR r50656 OR "renese r" OR "renese-r")

S7 (TX "pomaglumetad methionil" OR "ly 2140023" OR ly2140023 OR compazine OR prochlORperazine OR "6140 rp" OR antinaus OR "bayer a 173" OR "bayer 173" OR capazine OR chlORMepazine OR chlORpeazine OR chlORperazine OR compro OR dicopal OR emelent OR klometil OR kronocin OR meterazine OR metherazine OR nautisol OR nipodal OR nORMalmin OR pasotomin OR prochlOR OR prochlORpemazine OR prochlORperacine OR prochlORperzine OR prochlORpromazine OR proclORperazine OR procot OR "rp 6140 ir rp6140" OR "sk and f 4657" OR "skf 4657" OR skf4657 OR tementil OR temetil OR buccastem OR dhaperazine OR emeteral OR emetiral OR nibromin OR proclozine OR procomp OR stemetil OR stemzine OR Profenamine OR dibutil OR ethopropazine OR etopropazine OR isothazine OR isothiazine OR lysivane OR parcidol OR pardisol OR parfezin\* OR parkisol OR parphezin OR parsidol OR parsitan OR phenopropazine OR "profenamine hydrochlORide" OR prophenamine OR rochipel OR rodipal OR "rp 3356" OR "sc 2538" OR promazine OR alofen OR alophen OR ampazine OR amprazim OR centractyl OR delazin OR esparin OR lete OR liranol OR "neo hibernex" OR neuroplegil OR piarine OR prazine OR "pro tan" OR promantine OR promanyl OR promilene OR promwill OR protactil OR protactyl OR romthiazine OR romtiazin OR "rp 3276" OR sediston OR sinophenin\* OR sparine OR tomil OR varophen OR verophen OR "wy 1094" OR (propantheline N4 thiopropazate) OR "pro-banthine" OR propiomazine OR "cb 1678" OR cb1678 OR largon OR propionylpromethazine OR propriomazine OR propromazine OR dORevane OR indORm OR phenocetyl OR propavan OR "wy 1359" OR propionylpromazine OR combelen OR dipropiomazine OR propiopromazine OR tranvet OR prothipendyl OR "ay 5603" OR ay5603 OR azacon OR "d 206" OR d206 OR dominal OR inalFORte OR largophren OR "lg 206" OR lg206 OR phrenotropin OR prothipendil OR protipendil OR protipendyl OR timovan OR tolnate OR tumovan OR protoveratrine OR "veralba r" OR verapene OR "protalba-r" OR pyrobutamine OR (sandril N2 pyronil) OR quinethazone OR hydromax OR raclopride OR "flb-472" OR "flb 472" OR "fla-870" OR "fla 870" OR flb472 OR fla870 OR "a 40664" OR a40664 OR remoxipride OR fla731 OR "fla-731")

S8 (TX Reserpine OR abten OR alkarau OR alserin OR anquil OR apoplon\* OR austrapine OR boiserpine OR crystoserpin OR crystoserpine OR elserpine OR eroseprin OR eskaserp OR evraloid OR hiserpia OR hypersine OR kogluoid OR lemiserp OR maviserp OR "neo antitensol" OR quiescin OR "r-e-s" OR "rau sed" OR "rau-sed" OR raudixoid OR rauloydin OR raunervil OR raupina OR raurine OR roused OR rousedan OR rousedyl OR rauserpine OR rausingle OR rautensin OR rauwilid OR rauwiloid OR rauwolfaf OR repoid OR resercen OR reserpamed OR reserpen OR reserpene OR reserpex OR reserpil OR reserpine OR reserpoid OR resine OR riserpa OR rivasin OR roxel OR roxinoid OR sandril OR sedaraupin OR serfin OR serfolia OR serolfia OR serpalan OR serpanray OR serpasil OR serpasol OR serpate OR serpen OR serpena OR serpentina OR serpiloid OR serpine OR serpivite OR sertabs OR sertensin OR sertina OR "vio serpine" OR "vio-serpine" OR "v serp" OR butiserpine OR metatensin OR naquival OR rimcazole OR "bw 234" OR "bw 234u" OR bw234 OR bw234u OR risperidone OR belivon OR consta OR neripros OR noprenia OR "r 64766" OR r64766 OR "r-64766" OR riperidon OR risolept OR rispen OR risperdal OR rispid OR rispolet OR rizodal OR sequinan OR zargus OR zofredal OR ritanserin OR "r-55667" OR r55667 OR "r 55667" OR romergoline OR "fce 23884" OR fce23884 OR "ls 111871" OR ls111871 OR Savoxepine OR "cgp 19486" OR "cgp 19486a" OR cgp19486 OR cgp19486a OR cipazoxapine OR savoxapine OR "sb 773812" OR sb773812 OR seridopidine OR "acr 343" OR acr343 OR setoperone OR "r 52245" OR spiperone OR "r 5147" OR r5147 OR spioperidol OR spiopitan OR sulfORidazine OR inofal OR "tpn 12" OR sulpiride OR tepavil OR lebopride OR "vertigo meresa" OR pontiride OR sulperide OR ekilid OR sulp OR sulpOR OR "vertigo-meresa" OR dolmatil OR



digton oe aiglonyl OR guastil OR sulpitil OR meresa OR synedil OR deponerton OR arminol OR neogama OR eglonyl OR sulpivert OR "vertigo-neogama" OR desisulpid OR psicocen OR dogmatil OR "vertigo neogama" OR tefludazine OR "lu 18 012" OR "lu 18-012" OR "lu 18012" OR "lu18 012" OR "lu18-012" OR lu18012 OR thiopropazate OR artalan OR dartal OR dartalan OR dantan OR "sc 7105" OR thiopropazat OR thioproperazine OR "rp 7843" OR thioperazine OR majeptil OR mayeptil OR vontil)

S9 (TX thiORidazine OR aldazine OR apothiORidazine OR calmaril OR mallORol OR mallORyl OR meleril OR mellaril OR mellerets OR mellerette\* OR melleril OR mellerzin OR melleryl OR melzine OR mepiozin OR ORsanil OR ridazin OR ridazine OR rideril OR sonapax OR thiomed OR thiORadazine OR thiORidacine OR thiORidazide OR thiORidazin OR thiORidazine OR thiORil OR thiosia OR thORidazine OR thiozine OR thiORidazineneurazpharm OR tiORidazin OR tiORidazine OR "tp 21" OR tpzl OR tiotixene OR cis thiothixene OR "cp 12,252 1" OR "cp 12252 1" OR "cp 122521" OR "cp12,252 1" OR cp12252 1 OR cp122521 OR navan OR navane OR "nsc 108165" OR nsc108165 OR onaven OR ORbinamon OR "p 4657 b" OR "p 4657b" OR "p4657b OR thiotixene OR thiotixin OR thiotixine OR thixit OR tiapride OR delpal OR "flo 1347" OR "flo-1347" OR flo1347 OR italprid OR sereprile OR thiapride OR tiapridal OR tiapridex OR tiaprizal OR equilibrium OR imiperone OR "dd 3480" OR dd3480 OR tolopelon OR (tranylcypromine N2 trifluoperazine) OR jatrosom OR parstelin OR stelapar OR triethylperazin\* OR trifluoperazine OR apotrifluoperazine OR calmazine OR eskazine OR eskazinyl OR espazine OR fluoperazine OR flupazine OR fluperin OR flurazin OR "iremo-pierol" OR jatroneural OR leptazine OR modalina OR modiur OR nerolet OR nylipton OR operzine OR oxyperazine OR psyrazine OR "skf 5019" OR spORalon OR stelazine OR terfluzin\* OR triflumed OR trifluoperazide OR trifluoperzine OR trifluperazine OR trifluORoperazine OR trifluORperacine OR trifluORperazine OR trifluperazine OR triflurin OR triftazin OR triftazine OR triftazinum OR trincalm OR triozone OR triptazine OR triphthasine OR triphthazine OR trifluperidol OR "mcn jr 2498" OR psicoperidol OR "r 2498" OR r2498 OR trifluoperidol OR triperidol OR trisedyl OR trisedil OR triflupromazine OR adazine OR fluopromazin OR fluopromazine OR fluORofen OR "mc 4703" OR mc4703 OR nivoman OR psyquil OR siquil OR "skf 4648 a" OR "skf 4648a" OR skf4648a OR trifluopromazine OR vespral OR vesprin OR vetame OR umespirone OR "kc 7218" OR "kc 9172" OR kc7218 OR kc9172 OR vabicaserin OR "sca 136" OR sca136 OR zetidine OR "dl 308" OR "dl 308 it" OR "dl 308it" OR dl308 OR dl308it OR zicronapine OR "lu 31 130" OR "lu 31-130" OR "lu31 130" OR "lu31-130" OR zoloperone OR "lr 511" OR lr511 OR zuclopenthixol OR clompenthixol OR cisORDinol OR sedanaxol OR zuclopenthixol OR clopixol)

S10 (TX adesipress OR arkamin OR atensina OR caprysin OR catapres OR catapresan OR catasan OR chlOFazolin OR chlOPhazolin OR chlOPhelin OR clinidine OR clofelin OR clofeline OR clomidine OR clondine OR clonicele OR clonidin OR clonidine OR clonipresan OR clonistada OR clonnirit OR clophelin OR clopheline OR daipres OR dcaï OR dichlORophenylaminoimidazoline OR dixarit OR duraclon OR haemiton OR hemiton OR hypodine OR isoglaucan OR jenloga OR kapvay OR "m 5041t" OR melzin OR nORMopresan OR nORMopresin OR paracefan OR "st 155" OR sulmidine OR taitecin OR "tenso timelet\*" OR MillicORten OR maxidex OR dexamethasone OR dexpak OR dexasone OR ORadexon OR hexadecadrol OR hexadrol OR methylfluORprednisolone OR decamet OR lORazepam OR idalprem OR sinestron OR ativan OR sedicepan OR duralozam OR ORfidal OR somagerol OR apolORazepam OR novolORazem OR laubeel OR donix OR wy4036 OR "wy 4036" OR "wy-4036" OR temesta OR nulORaz OR tolid OR midazolam OR "ro 21-3981" OR "ro 21 3981" OR versed OR "ro 213981" OR dORMicum OR DIAZEPAM OR diazemuls OR apaurin OR seduxen OR faustan OR sibazon OR valium OR stesolid OR relanium OR donepezil OR aricept OR aricept OR asenta OR "e 2020" OR "e2020" OR eranz OR memac OR memORit OR rivastigmine OR "ena 713" OR ena713 OR exelon OR nimvastid OR prometax OR rivastigmin OR "sdz 212 713" OR "sdz 212-713" OR "sdz 212713" OR "sdz ena 713" OR "sdz ena713" OR "sdz212 713" OR "sdz212-713" OR sdz212713)

S11 (TX "ay 23028" OR "ay-23028" OR ay23028 OR butaclamol OR butaperazine OR "ahr 3000" OR "bayer 1362" OR butaperazinum OR butyrylperazin OR butyrylperazine OR megalactil OR randoelectil OR randoelectyl OR repoise OR "riker 595" OR tytylen OR carfenazine OR carfenazinum OR carphenazine OR "nsc 71755" OR nsc71755 OR procethazine OR proketazine OR "wy 2445" OR wy2445 OR cariprazine OR "mp 214" OR mp214 OR "rgh 188" OR rgh188 OR carpipramine OR carbadipimidine OR defecton OR defekton OR prazinil OR "pz 1511" OR pz1511 OR "rp 21679" OR rp21679 OR carvotroline OR "wy 47791" OR wy47791 OR Centbutindole OR chlORothiazide OR "diupres-250" OR "diupres-500" OR chlORphenethazine OR chlORfenethazine OR elroquil OR marophen OR chlORproethazine OR neuriplege OR "rp 4909" OR rp4909 OR chlORpromazine OR "2601 a" OR aminasin OR aminasine OR aminazin OR aminazine OR ampliactil OR amplitil OR ancholactil OR aspersinal OR bellacina OR cepezet OR chlomazine OR chlORactil OR chlORazine OR chlORbromasin OR chlORdelazine OR chlORderazin OR chlORMazine OR chlORpromanyl OR chlORpromazin OR chlORpromed OR clonazine OR clORdelazin OR clORpromaz OR clORpromazine OR clozine OR contomin OR duncan OR elmarin OR esmino OR fenactil OR hibanil OR hibernal OR hibernal OR "hl 3746" OR "hl 5746" OR klORproman OR klORpromazin OR klORpromex OR laractyl OR largactil OR largactyl OR matcine OR megaphen OR megatil OR "ml 5746" OR neomazine OR neurazine OR novomazina OR phenathyl OR plegomazin OR plegomazine OR proma OR promacid)

S12 (TX promactil OR promapar OR promazil OR promexin OR propaphen OR propaphenin OR prozil OR prozin OR psychozine OR psynOR OR "rp 4560" OR sanopron OR "skf 2601 a" OR solidon OR sonazine OR tarocitil OR tarocitil OR "thOR prom"

OR thORazene OR thORazine OR tORazina OR winsumin OR wintamine OR wintermin OR zuledin OR "thORa-dex" OR opro-  
 mazine OR secotiL OR chlORprothixene OR chloprothixene OR "chlOR prothixene" OR chlORoprothixene OR chlORprothixen  
 OR chlORprothixenechlORide OR chlORprotixen OR chlORprotixene OR chlothixen OR "n 714" OR "n 7714" OR "ro 4 0403"  
 OR "ro 40403" OR taractan OR tarasan OR traquilan OR troxen OR truxal OR truxaleta OR truxaletten OR chlORprothixene OR  
 chloprothixene OR "chlOR prothixene" OR chlORoprothixene OR chlORprothixen OR chlORprothixenechlORide OR chlORpro-  
 tixen OR chlORprotixene OR chlothixen OR "n 714" OR "n 7714" OR "ro 40403" OR taractan OR tarasan OR traquilan OR troxen  
 OR truxal OR truxaleta OR truxaletten OR cinuperone OR "hr 375" OR hr375 OR clocapramine OR "y 4153" OR y4153)  
 S13 (TX zapen OR zaponex OR cyamemazine OR cianatil OR cyamepromazine OR "fi 6229" OR fi6229 OR kyamepromazin  
 OR "rp 7204" OR rp7204 OR tercián OR prochlorperazine OR "eskatrol spansule" OR (diethylstilbestrol N2 methyltestosterone)  
 OR tylandril OR dimetotiazine OR banistyl OR dimethiotazine OR dimethiothazine OR dimethothiazine OR dimethotiazine ro  
 dimetiotazine OR fonazine OR "il 6302" OR (dimeamide N2 phenobarbital) OR dixyrazine OR dixirazine OR dixyrazin OR  
 dyxirazine OR esocalm OR esucos OR metronal OR roscal OR "ucb 3412" OR ucb3412)  
 S14 (TX clopipramine OR cremin OR mosapramine OR y516 OR clotiapine OR clothiapiñ OR clothiapiñ OR entumin\* OR "hf  
 2159" OR hf2159 OR "cp 903397" OR cp903397 OR alemoxan OR azaleptin OR clopine OR clopsine OR clozapin\* OR clozaril  
 OR denzapine OR dORval OR dozapine OR elcrit OR fazaclo OR "hf 1854" OR hf1854 OR lapenax OR leponex OR lozapin\* OR  
 sizopin OR versacloz OR "wander compound")  
 S15 (TX "cloflumide mesylate" OR "vufb 15496" OR vufb15496 OR clofluperol OR seperidol OR clopenthixol OR "ay 62021" OR  
 ay62021 OR chlorpenthixol)  
 S16 (MH "Antipsychotic Agents, Phenothiazine") OR (MH "Antipsychotic Agents") OR (MH "Antipsychotic Agents, Butyrophenone")  
 OR (MH "Azaperone") OR (MH "Droperidol") OR (MH "Haloperidol") OR (MH "Ziprasidone") OR (MH "Chlorpromazine") OR  
 (MH "Fluphenazine") OR (MH "Perphenazine Hydrochloride") OR (MH "Prochlorperazine") OR (MH "Thioridazine") OR (MH  
 "Trifluoperazine Hydrochloride") OR (MH "Aripiprazole") OR (MH "Clozapine") OR (MH "Asenapine") OR (MH "Iloperidone")  
 OR (MH "Molindone Hydrochloride") OR (MH "Loxapine") OR (MH "Olanzapine") OR (MH "Olanzapine-Fluoxetine") OR (MH  
 "Ondansetron") OR (MH "Paliperidone") OR (MH "Quetiapine") OR (MH "Thiothixene") OR (MH "Risperidone")  
 S17 (TX antipsychotic\* OR neuroleptic\* OR (major N2 tranquili\*))  
 S18 (TX aceperone OR acetabutone OR acetobutone OR "r 3248" OR r3248 OR acepromazine OR acetopromazine OR vetranquil  
 OR acetylpromazine OR acepromazine OR calmivet OR acetazine OR notensil OR plegicil OR promace OR soprintin OR anatan  
 OR anergan OR atravet OR "cb 1522" OR cb1522 OR plegicin OR plegicil OR sedalin OR soprontin OR aceprometazine OR  
 acepromethazine OR acetylpromethazine OR acetophenazine OR acephenazine OR "nsc 70600" OR nsc70600 OR "sch 6673" OR  
 sch6673 OR tindal OR adopraxine OR adopraxin OR "slv 313" OR slv313 OR alimemazin OR alimemasine OR alimemazin\*  
 OR alimezine or "bayer 1219" or electrotrimeprazine or methylpromazine or palpex or "rp 6549" or rp6549 OR trimeprazine OR  
 trimeprezine OR varialgil OR nedeltran OR panectyl OR repeltin OR temaril OR temaryl OR teralen OR teralene OR theralen OR  
 theralene OR valergan OR vallergeran OR "bms 181100" OR bms181100 OR "bmy 14802" OR "bmy 14802 1" OR "bmy 14802-1"  
 OR bmy14802 OR "bmy14802 1" OR "bmy14802-1" OR bmy148021 OR "s 16924" OR s16924 OR amitrypline OR perphenazine  
 OR "anxipress-d" OR "duo-vil 2-10" OR "duo-vil 2-25" OR "duo-vil 4-10" OR etrafon OR etraphon OR longopax OR mutabon  
 OR mutanxion OR mutaspline OR "neuragon-a" OR "neuragon-b" OR peritriptyl OR polybon OR triavil OR triptafen)  
 S19 (TX aplindORE OR "dab 452" OR dab452 OR palindORE OR "way dab 452" OR "way dab452" OR abaperidone OR "fi  
 8602" OR fi8602 OR alentamol OR alentemol OR "u 66444b" OR "u 68552b" OR "u 68553b" OR u66444b OR u68552b OR  
 u68553b OR aminosultopride OR amisulpiride OR amisulpridum OR "dan 2163" OR dan2163 OR sertol OR socian OR solian OR  
 amperozide OR "fg 5606" OR fg5606 OR aripiprazole OR abilify OR abilitat OR "opc 14597" OR opc14597 OR r asenapine OR  
 "ORg 5222" OR ORg5222 OR saphris OR sycrest OR batelapine OR "cgs 13429" OR cgs13429 OR belaperidone OR balaperidone  
 OR "lu 111995" OR lu111995 OR bifeprunox OR "du 127090" OR du127090 OR emonapride OR emirace OR nemonapride  
 OR "ym 09151" OR "ym 09151 02" OR "ym 09151 2" OR "ym 09151-02" OR "ym 09151-2" OR ym09151 OR "ym09151 02"  
 OR "ym09151 2" OR "ym09151-02" OR "ym09151-2" OR ym0915102 OR ym091512 OR elopiprazole OR flumezapine OR "ly  
 120363" OR ly120363 OR fluoxetine OR symbya OR hp873 OR "ilo 522" OR ilo522 OR zomaril OR lurasidone OR latuda OR  
 "mk 3756" OR mk3756 OR "sm 13496" OR sm13496 OR "smp 13496" OR smp13496 OR melperone OR bunil OR buronil OR  
 eunerpan OR "fg 5111" OR fg5111 OR flubuperone OR melperon OR methylperone OR metylperone OR metylperonum OR "sdz  
 208 912" OR "sdz 208-912" OR "sdz 208912" OR "sdz 912" OR "sdz hdc 912" OR "sdz hdc912" OR "sdz208 912" OR "sdz208-  
 912" OR sdz208912 OR sdz912 OR "sdz 208 911" OR "sdz 208-911" OR "sdz 208911" OR "sdz 911" OR "sdz hac 911" OR  
 "sdz hac911" OR "sdz208 911" OR "sdz208-911" OR sdz208911 OR sdz911 OR "fg 5803" OR fg5803 OR nORclozapine OR  
 demethylclozapine OR desmethylclozapine OR ocaperidone OR "r 79598" OR r79598 OR olanzapine OR anzatric OR "dopin tab"  
 OR "jolyon md" OR lanopin OR lanzac OR "ly 170053" OR ly170053 OR meltolan OR midax OR olace OR oladay OR olan  
 OR olandus OR olanex OR olansek OR olapin OR olazax OR oleanz OR olexar OR oltal OR olzap OR onza OR "ozapin md" OR

psychozap OR relprev OR zalasta OR zelta OR zydis OR zypadhera OR zyprex OR zyprexa OR zyprexav OR paliperidone OR invega  
 OR "paliperidone palmitate" OR "r 76477" OR r76477 OR "ro 76477" OR "ro 92670" OR ro76477 OR ro92670 OR xelplion OR  
 panamesine OR "emd 57445" OR emd57445 OR pentiapine OR "cgs 10746" OR cgs10746 OR "cgs 10746b" OR cgs10746b OR  
 perlapine OR "aw 14'2333" OR "aw 142333" OR aw142333 OR perlapin OR perospirone OR lullan OR "sm 9018" OR sm9018  
 OR pridopidine OR "acr 16" OR acr16 OR "asp 2314" OR asp2314 OR "fr 310826" OR fr310826 OR huntexil OR quetiapine OR  
 "ici 204636" OR "ici 204646" OR ici204636 OR ici204646 OR seroquel OR socalm OR tienapine OR remoxipride OR "a 33547"  
 OR a33547 OR "fla 731" OR fla731 OR roxiam OR rilapine OR sertindole OR "lu 23174" OR lu23174 OR "s 1991" OR s1991  
 OR serdolect OR serlect OR sulpiride OR abilit OR aiglonyl OR arminol OR dobren OR dogmatil OR dogmatyl OR dolmatil OR  
 eglonyl OR equilid OR "fk 880 " OR fk880 OR isnamide OR levobren OR levopraid OR levosulpiride OR meresa OR miradol OR  
 neogama OR sulfiride OR sulpivert OR sulpyride OR synedil OR vipral OR sultopride OR barnetil OR barnotil OR "ms 5024" OR  
 ms5024 OR sulfopride OR tenilapine OR tiospirone OR "bmy 13859" OR bmy13859 OR "mj 13859" OR "mj 13859 1" OR "mj  
 13859-1" OR mj13859 OR "mj13859 1" OR "mj13859-1" OR mj138591 OR tiaspirone OR volinanserin OR "m 100907" OR  
 m100907 OR "mdl 100151" OR "mdl 100907" OR mdl100151 OR mdl100907 OR ziprasidone OR "cp 88059" OR "cp 88059  
 01" OR "cp 88059 27" OR "cp 88059-01" OR "cp 88059-27" OR "cp 8805901" OR "cp 8805927" OR cp88059 OR "cp88059  
 01" OR "cp88059 27" OR "cp88059-01" OR "cp88059-27" OR cp8805901 OR cp8805927 OR geodon OR zeldox OR zeldrox OR  
 zipsydon OR zotepine OR lodopin OR nipolept OR azaperone OR "r-1929" OR r1929 OR sedaperone OR stresnil OR benperidol  
 OR anquil OR benperidone OR benzoperidol OR benzperidol OR benperidolneuraxpharm OR "cb 8089" OR cb8089 OR frenactyl  
 OR frenactil OR glianimon OR "mcn jr 4584" OR "mcn jr4584" OR phenactil OR "r 4584" OR r4584 OR berupipam OR "nnc  
 22 0010" OR "nnc22 0010" OR bitopertin OR paliflutine OR "r 1678" OR r1678 OR "rg 1678" OR rg1678 OR "ro 4917838"  
 OR ro4917838 OR blonanserin OR "ad 5423" OR ad5423 OR lonasen OR brexpiprazole OR "opc 34712" OR opc34712 OR  
 brofoxine OR dimetabrone OR "fi 6820" OR fi6820 OR bromospiperone OR bromospiroperidol OR bromperidol OR impromen  
 OR "r 11,333" OR "r 11333" OR "r11,333" OR r11333 OR tesoprel OR "impromen decanoate" OR "r 46,541" OR "r 46541" OR  
 "r46,541" OR r46541)  
 S20 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR  
 S17 OR S18 OR S19  
 S21 (MH "Confusion") OR (MH "Delirium") OR (MH "Psychomotor Agitation") OR (MH "Hallucinations") OR (MH "Charles  
 Bonnet Syndrome") OR (MH "Illusions") OR (MH "ICU Psychosis") OR (MH "Paranoid Disorders") OR (MH "Delirium, Dementia,  
 Amnestic, Cognitive Disorders") OR (MH "Psychotic Disorders")  
 S22 (TX inattention OR inattentive\* OR "icu syndrome" OR (intensive N2 care N2 syndrome) OR "acute brain dysfunction" OR  
 (acute N2 brain N2 dysfunction\*) OR "septic encephalopath\*" OR "acute brain failure" OR "acute organic psychosyndrome\*" OR  
 "acute brain syndrome" OR "metabolic encephalopath\*" OR "acute psycho-organic syndrome\*" OR "clouded state" OR "clouding of  
 consciousness" OR "exogenous psychosis" OR "toxi psychosis" OR "icu psychosis")  
 S23 (MH "Brain Diseases") AND ( (MH "Catastrophic Illness") OR (MH "Critical Illness") OR (MH "Critically Ill Patients") OR  
 (MH "Sepsis") )  
 S24 (MH "Brain Diseases") AND ((MH "Intensive Care Units") OR (MH "Coronary Care Units") OR (MH "Respiratory Care Units")  
 OR (MH "Stroke Units") OR (MH "Critical Care"))  
 S25 (MH "Brain Diseases") AND ( (MH "Hospitalization") OR (MH "Length of Stay") OR (MH "Patient Admission") OR (MH  
 "Patient Discharge") OR (MH "Readmission") ) )  
 S26 S21 OR S22 OR S23 OR S24 OR S25  
 S27 S20 AND S26 [\*\*\*\*Base clinical set\*\*\*\*]  
 S28 (MH "Clinical Trials+")  
 S29 S27 AND S28 [\*\*\*\*Clinical trial results\*\*\*\*]

## Appendix 5. Thomson Reuters Web of Science Search Strategy

Database: Thomson Reuters Web of Science (July 20, 2017)

Search Strategy:

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH Timespan=All years

#1 TS=(dolasetron OR anemet OR anzemet OR “mdl 73147” OR “mdl 73147ef” OR mdl73147 OR mdl73147ef OR zamanon OR droperidol OR dehidrobenzoperidol OR dehydrobenzoperidol OR dehydrobenzoperiol OR dehydrobenzperidol OR dehydrobenzperidolum OR dridol OR droleptan OR droperol OR halkan OR inaprine OR inapsin OR inapsine OR “mcn jr 4749” OR “mcn r 4749” OR ORidol OR “r 4749” OR sintodian OR troperidol OR xomolix OR innovan OR innovar OR inoval OR inovar OR talamonal OR thalamonal OR disifelit)

#2 TS=(dolasetron OR anemet OR anzemet OR “mdl 73147” OR “mdl 73147ef” OR mdl73147 OR mdl73147ef OR zamanon OR droperidol OR dehidrobenzoperidol OR dehydrobenzoperidol OR dehydrobenzoperiol OR dehydrobenzperidol OR dehydrobenzperidolum OR dridol OR droleptan OR droperol OR halkan OR inaprine OR inapsin OR inapsine OR “mcn jr 4749” OR “mcn r 4749” OR ORidol OR “r 4749” OR sintodian OR troperidol OR xomolix OR innovan OR innovar OR inoval OR inovar OR talamonal OR thalamonal OR disifelit OR duoperone OR “ahr 6646” OR ahr6646 OR (ephedrine N2 sulfate) OR renir OR Estrosed OR sergynol OR etymemazine OR diquel OR ethotrimprazine OR ethylisobutrazine OR ethymemazine OR nital OR “rp 6484” OR rp6484 OR sergetyl OR etazolate OR sq20009 OR “sq-20009” OR “sq 20009” OR Farampat OR OR “cx 691” OR cx691 OR “ORg 24448” OR ORg24448 OR fluanisone OR “anti pica” OR antipica OR fluanison\* OR fluanizone OR fluoanisone OR haloanison OR haloanisone OR “md 2028” OR md2028 OR “r 2028” OR “r 2167” OR r2028 OR r2167 OR sedalande OR sedalanide OR solusediv)

#3 TS=(flupentixol OR flupenthixol\* OR emergil OR fluanxol OR fluxanxol OR siplaril OR siplarol OR depixol OR viscoleo OR fluphenazin\* OR anatensil OR anatenzol OR antasol OR cenilene OR dapotum OR elinol OR flufenan OR flufenazine OR flumezin OR fluORfenazine OR fluphenacin OR “fluzine-p” OR frORphenazine OR lyogen OR lyORodin OR moditen OR moditin OR omca OR pacinol OR permitil OR phth OR phenazine OR potensone OR prolixan OR prolixene OR prolixin\* OR “s 94” OR sevinol OR squaline OR squalon\* OR siquoline OR sq4918 OR tensofin OR trancin OR valamina OR vespazin\* OR “dapatum d25” OR dapotum OR decafen OR flucan OR fludecasine OR fludecate OR lyogen OR mirenil OR modicate OR phlufdek OR sydepres OR flunanthate OR fluspirilene OR fluspi OR fluspirilen OR imap OR r6218 OR redeptin)

#4 TS=(spirodiflamine OR kivat OR Flutroline OR “cp 36584” OR “cp36,584” OR cp36584 OR “org 5878” OR org5878 OR gevetroline OR “wy 47384” OR wy47384 OR penite OR haloperidol OR alased OR aloperidin\* OR avant OR binison OR brotopon OR celenase OR cereen OR cerenace OR cizORen OR depidol OR dozic OR duraperidol OR “einalon s” OR fORTunan OR govotil OR haldol OR halidol OR “halo-p” OR halojust OR halomed OR haloneural OR haloper OR haloperil OR haloperin OR haloperitol OR halopidol OR halopol OR halosten OR haricon OR “haridol-d” OR keselan OR linton OR “lodomer-2” OR “mcn jr 1625” OR “mcn jr1625” OR mixidol OR novoperidol OR “nsc 170973” OR nsc170973 OR peluces OR perida OR peridol OR peridOR OR “r 1625” OR r1625 OR selezyme OR seranace OR serenace OR serenase OR serenelfi OR siegoperidol OR sigaperidol OR trancodol OR pericate OR “r 13,672” OR “r 13672” OR senORm OR hexamethonium OR reserthonium OR dralserp OR (hydralazine N2 reserpine) OR “serpasil-apresoline” OR “hydropresOR dichlotride s” OR “hydro-reserp” OR hydrochlORothiazide OR hydroserpine OR “medeserpine co” OR “serpasil-esidrix” OR butiserpazide OR rautraX OR salutensin\* OR isofloxythepin OR “vufb 10662” OR isomolpan OR “cgs 15855” OR “cgs 15855 a” OR “cgs 15855a” OR cgs15855 OR cgs15855a OR (isopropamide N4 prochlORperazine) OR “combid spansule” OR lenperone OR “ahr 2277” OR ahr2277 OR elanone OR levomepromazine OR “apo-methoprazine” OR “bayer 1213” OR “cl 36467” OR “cl 39743” OR cl36467 OR cl39743 OR hirnamin OR mepromazine OR levium OR promazine OR levomeprazine OR levopromazin\* OR levoprome OR levozin OR mepromazine OR methotrimprazine OR methozane OR milezin OR minozinan OR neozine OR neuractil OR neurocil OR nirvan OR nozinan OR “rp 7044” OR rp7044 OR sinogan OR “skf 5116” OR skf5116 OR tiscerin OR tiscerin OR veractil)

#5 TS=(lithium OR loxapine OR adasuve OR “alz 004” OR alz004 OR “az 004” OR az004 OR “cl 62,362” OR “cl 62362” OR “cl62,362” OR cl62362 OR “cl 71563” OR “cl-71563” OR cl71563 OR loxapinsuccinate OR cloxazepin\* OR loxapane OR loxapin\* OR loxitane OR oxilapine OR “sum 3170” OR sum3170 OR daxolin OR desconex OR loxapac OR maroxepine OR mazapertine OR “rwj 37796” OR rwj37796 OR mepiprazole OR “emd 16923” OR emd16923 OR psigodal OR prozine OR meprobamate OR mesORidazin\* OR esORidazine OR lidanar OR lidanil OR mesORin OR “nc 123” OR (thiORidazine N2 sulfoxide) OR “tps 23” OR serentil OR (methamphetamine N2 reserpine) OR methiothepin\* OR metitepine OR methopromazine OR methoxypromazine OR metopromazine OR “diutensen-r” OR levopromazine OR tizercine OR methotrimprazine OR levomepromazine OR levomeprazin OR tiscerin OR tizertsin)

#6 TS=(metofenazate OR frenolon OR metaphenazine OR methophenazine OR metophenazine OR phrenolon OR molindon\* OR “en 1733a” OR en1733a OR lidone OR moban OR molindOR OR moperone OR luvatren OR luvatrena OR “methyl peridol” OR

methylperidol\* OR moperon OR "r 1658" OR "y 20024" OR y20024 OR "Alx 5407" OR alx5407 OR NFPS OR "sb 277011" OR "sb 277011a" OR sb277011 OR sb277011a OR neboglamine OR "cr 2249" OR cr2249 OR "xy 2401" OR xy2401 OR (nicotinic N4 pentetrazole N4 reserpine) OR (nicozol N2 reserpine) OR noctran OR ORchlORpromazine OR demethylchlORpromazine OR demonomethylchlORpromazine OR desmethylchlORpromazine OR desmonomethylchlORpromazine OR monodesmethylchlORpromazine OR ondansetron OR gr38032f OR "gr 38032f" OR "sn 307" OR sn307 OR "gr-38032f" OR "sn-307" OR zofran OR oxiperomide OR "r 4714" OR r4714 OR oxyptertin\* OR "cl 77328" OR cl77328 OR equipertine OR fORit OR opertil OR oxipertin OR oxyptertin OR "win 18501 2" OR "win 18501-2" OR "win 185012" OR "win18501 2" OR "win18501-2" OR win185012 OR oxyprothepine OR oxyprothepin OR pecazine OR lacumin OR mepasin OR mepazine OR nothiazine OR "p 391" OR pacatal OR pacatol OR pactal OR papital OR paxital OR pecazine OR "w 1224" OR penfluridol OR "mcn jr 16341" OR micefal OR "r 16341" OR semap OR "r 16341" OR "r-16341" OR r16341 OR perazine OR taxilan)

#7 TS=(pentaerythrityl OR pentaserpine OR respet OR pentraline OR "nambu-serpine" OR (pentobarbital N2 reserpine) OR perazine OR "p 725" OR pernazine OR taxilan OR periciazine OR aolept OR neulactil OR neuleptil\* OR periciazinum OR pericyazine OR propericiazine OR propericiazin OR propericiazine OR "rp 8909" OR "skf 20716" OR perimetazine OR "1317 an" OR "an 1317" OR an1317 OR lepryl OR perimethazine OR perphenazine OR chlORperphenazine OR chlORpiprazine OR chlORpiprozone OR decentan OR etaperazine OR ethaperazine OR "f-mon" OR fentazin OR leptopsique OR peratsin OR perfenazine OR perferazine OR pernamed OR perphenan OR perphenazin\* OR "perzine-p" OR pORazine OR "sch 3940" OR thilatazin OR tranquisan OR trifalon OR trilafan OR trilafon OR trilifan OR triliphan OR triomin OR "pf 217830" OR pf217830 OR "pf 2400013" OR pf2400013 OR "pf 3463275" OR pf3463275 OR (phenobarbital N2 reserpine) OR "solfo-serpine" OR bromoserpin OR "theo-serp" OR "theobarb-r" OR theoserpin OR besertal OR "neo-slowten" OR Picobenzide OR dosetil OR "m 14012 4" OR "ma 14012" OR picobenzamide OR piflutixol OR pimavanserin OR "acp 103" OR acp103 OR pimethixene OR "bp 400" OR "bp 400 e" OR "bp 400e" OR bp400 OR bp400e OR muricalm OR pimetixin OR pimoze OR antalon OR "mcn jr 6238" OR opiran OR ORap OR pimocide OR pimORide OR pinozide OR pizide OR "r 6238" OR r6238 OR pipamperone OR dipeperon OR dipiperon OR "dl piperonyl" OR flORopipamide OR "piperonyl of pripamperone of r 3345" OR r3345 OR piperacetazine OR "pc 1421OR pc1421" OR quide OR pipotiazine OR "9366 rp" OR pipORtil OR pipothiazine OR "rp 19366" OR rp19366 OR "il 19552" OR il19552 OR "rp 19552" OR rp19552 OR rp 19551 OR pirenperone OR "r 47465" OR "r 50656" OR r47465 OR r50656 OR "renese r" OR "renese-r")

#8 TS=("pomaglutetad methionil" OR "ly 2140023" OR ly2140023 OR compazine OR prochlORperazine OR "6140 rp" OR antinaus OR "bayer a 173" OR "bayer 173" OR capazine OR chlORMepazine OR chlORpeazine OR chlORperazine OR compro OR dicopal OR emelent OR kometil OR kronocin OR meterazine OR methetazine OR nautisol OR nipodal OR nORMalmin OR pasotomin OR prochlOR OR prochlORpemazine OR prochlORperacine OR prochlORperzine OR prochlORpromazine OR proclORperazine OR procot OR "rp 6140 ir rp6140" OR "sk and f 4657" OR "skf 4657" OR skf4657 OR temetil OR temetil OR buccastem OR dhaperazine OR emeteral OR emetiral OR nibromin OR proclozine OR procomp OR stemetil OR stemzine OR Profenamine OR dibutil OR ethopropazine OR etopropazine OR isothazine OR isothiazine OR lysivane OR parcidol OR pardisol OR parfezin\* OR parkisol OR parphezin OR parsidol OR parsitan OR phenopropazine OR "profenamine hydrochlORide" OR prophenamine OR rochipel OR rodipal OR "rp 3356" OR "sc 2538" OR promazine OR alofen OR alophen OR ampazine OR amprazim OR contractyl OR delazin OR esparin OR lete OR liranol OR "neo hibernex" OR neuroplegil OR piarine OR prazine OR "pro tan" OR promantine OR promanyl OR promilene OR promwill OR protactil OR protactyl OR romthiazine OR romthiazin OR "rp 3276" OR sediston OR sinophen\* OR sparine OR tomil OR varophen OR verophen OR "wy 1094" OR (propantheline N4 thiopropazate) OR "pro-banthine" OR propiomazine OR "cb 1678" OR cb1678 OR largon OR propionylpromethazine OR propriomazine OR propromazine OR dORevane OR indORm OR phenoctyl OR propavan OR "wy 1359" OR propionylpromazine OR combelen OR dipropiomazine OR propiopromazine OR tranvet OR prothipendyl OR "ay 5603" OR ay5603 OR azacon OR "d 206" OR d206 OR dominal OR inalFORte OR largophren OR "lg 206" OR lg206 OR phrenotropin OR prothipendil OR protipendil OR protipendyl OR timovan OR tolnate OR tumovan OR protoveratrine OR "veralba r" OR verapene OR "protalba-r" OR pyrrobutamine OR (sandril N2 pyronil) OR quinethazone OR hydromax OR raclopride OR "flb-472" OR "flb 472" OR "fla-870" OR "fla 870" OR flb472 OR fla870 OR "a 40664" OR a40664 OR remoxipride OR fla731 OR "fla-731")

#9 TS=(Reserpine OR abten OR alkarau OR alserin OR anquil OR apopl\* OR austrapine OR boiserpine OR crystoserpin OR crystoserpine OR elserpine OR eroseprin OR eskaserp OR evraloid OR hiserpia OR hypersine OR koglucoide OR lemiserp OR maviserp OR "neo antitensol" OR quiescin OR "r-e-s" OR "rau sed" OR "rau-sed" OR raudixoid OR rauloydin OR raunvill OR raupina OR raurine OR roused OR rousedan OR rousedyl OR rauserpine OR rausingle OR rautensin OR rauwilid OR rauwiloid OR rauwolfaf OR repoid OR resercen OR reserpamed OR reserpen OR reserpene OR reserpex OR reserpil OR reserpine OR reserpoid OR resine OR riserpa OR rivasin OR roxel OR roxinoid OR sandril OR sedaraupin OR serfin OR serfolia OR serolfia OR serpalan OR serpanray OR serpasil OR serpasol OR serpate OR serpen OR serpena OR serpentina OR serpiloid OR serpine OR serpivite OR sertabs OR sertensin OR sertina OR "vio serpine" OR "vio-serpine" OR "v serp" OR butiserpine OR metatensin OR naquival OR rimcazole OR "bw 234" OR "bw 234u" OR bw234 OR bw234u OR risperidone OR belivon OR consta OR neripros OR noprenia OR "r

Antipsychotics for treatment of delirium in hospitalised non-ICU patients (Review)  
Copyright © 2018 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

clozine OR contomin OR duncan OR elmarin OR esmino OR fenactil OR hibanil OR hibernal OR hibernol OR "hl 3746" OR "hl 5746" OR klORproman OR klORpromazin OR klORpromex OR laractyl OR largactil OR largactyl OR matcine OR megaphen OR megatil OR "ml 5746" OR neomazine OR neurazine OR novomazina OR phenathyl OR plegomazin OR plegomazine OR proma OR promacid)

#13 TS=(promactil OR promapar OR promazil OR promexin OR propaphen OR propaphenin OR prozil OR prozin OR psychozine OR psynOR OR "rp 4560" OR sanopron OR "skf 2601 a" OR solidon OR sonazine OR taroctil OR taroctyl OR "thOR prom" OR thORazene OR thORazine OR tORazina OR winsumin OR wintamine OR wintermin OR zuledin OR "thORa-dex" OR opro-mazine OR secotiL OR chlORprothixene OR chloprothixene OR "chlOR prothixene" OR chlORoprothixene OR chlORprothixen OR chlORprothixenechlORide OR chlORprotixen OR chlORprotixene OR chlothixen OR "n 714" OR "n 7714" OR "ro 4 0403" OR "ro 40403" OR taractan OR tarasan OR traquilan OR troxen OR truxal OR truxaleta OR truxaletten OR chlORprothixene OR chloprothixene OR "chlOR prothixene" OR chlORoprothixene OR chlORprothixen OR chlORprothixenechlORide OR chlORprotixen OR chlORprotixene OR chlothixen OR "n 714" OR "n 7714" OR "ro 40403" OR taractan OR tarasan OR traquilan OR troxen OR truxal OR truxaleta OR truxaletten OR cinuperone OR "hr 375" OR hr375 OR clocapramine OR "y 4153" OR y4153)

#14 TS=(zapen OR zaponex OR cyamemazine OR cianatil OR cyamepromazine OR "fi 6229" OR fi6229 OR kyamepromazin OR "rp 7204" OR rp7204 OR tercian OR prochlORperazine OR "eskatrol spansule" OR (diethylstilbestrol N2 methyltestosterone) OR tylandril OR dimetotiazine OR banistyl OR dimethiotazine OR dimethiothazine OR dimethothiazine OR dimethotiazine ro dimetiotazine OR fonazine OR "il 6302" OR (dimevamide N2 phenobarbital) OR dixyrazine OR dixirazine OR dixyrazin OR dyxirazine OR esocalm OR esucos OR metronal OR roscal OR "ucb 3412" OR ucb3412)

#15 TS=(clopipramine OR cremin OR mosapramine OR y516 OR clotiapine OR clothiapi OR clothiapine OR entumin\* OR "hf 2159" OR hf2159 OR "cp 903397" OR cp903397 OR alemoxan OR azaleptin OR clopine OR clopsine OR clozapin\* OR clozaril OR denzapine OR dORval OR dozapine OR elcrit OR fazaclo OR "hf 1854" OR hf1854 OR lapenax OR leponex OR lozapin\* OR sizopin OR versacloz OR "wander compound")

#16 TS=("cloflumide mesylate" OR "vufb 15496" OR vufb15496 OR clofluperol OR seperidol OR clopenthixol OR "ay 62021" OR ay62021 OR chlorpenthixol)

#17 TS=(antipsychotic\* OR neuroleptic\* OR (major N2 tranquili\*))

#18 TS=(aceperone OR acetabutone OR acetobutone OR "r 3248" OR r3248 OR acepromazine OR acetopromazine OR vetranquil OR acetylpromazine OR acepromazine OR calmivet OR acetazine OR notensil OR plegicil OR promace OR soprintin OR anatan OR anergan OR atravet OR "cb 1522" OR cb1522 OR plegicin OR plegicyl OR sedalin OR soprontin OR aceprometazine OR acepromethazine OR acetylpromethazine OR acetophenazine OR acephenazine OR "nsc 70600" OR nsc70600 OR "sch 6673" OR sch6673 OR tindal OR adopraxine OR adopraxin OR "slv 313" OR slv313 OR alimemazin OR alimemasine OR alimemazin\* OR alimezine or "bayer 1219" or electrotrimeprazine or methylpromazine or palpex or "rp 6549" or rp6549 OR trimeprazine OR trimeprezine OR varialgil OR nedeltran OR panectyl OR repeltin OR temaril OR temaryl OR teralen OR teralene OR theralen OR theralene OR valergan OR vallergeran OR "bms 181100" OR bms181100 OR "bmy 14802" OR "bmy 14802 1" OR "bmy 14802-1" OR bmy14802 OR "bmy14802 1" OR "bmy14802-1" OR bmy148021 OR "s 16924" OR s16924 OR amitrypline OR perphenazine OR "anxipress-d" OR "duo-vil 2-10" OR "duo-vil 2-25" OR "duo-vil 4-10" OR etrafon OR etraphon OR longopax OR mutabon OR mutanxion OR mutaspline OR "neuragon-a" OR "neuragon-b" OR peritriptyl OR polybon OR triavil OR triptafen)

#19 TS=(aplindORE OR "dab 452" OR dab452 OR palindORE OR "way dab 452" OR " way dab452" OR abaperidone OR "fi 8602" OR fi8602 OR alentamol OR alentemol OR "u 66444b" OR "u 68552b" OR "u 68553b" OR u66444b OR u68552b OR u68553b OR aminosultopride ORamisulpiride OR amisulpridum OR "dan 2163" OR dan2163 OR sertol OR socian OR solian OR amperozide OR "fg 5606" OR fg5606 OR aripiprazole OR abilify OR abilitat OR "opc 14597" OR opc14597 ORr asenapine OR "ORg 5222" OR ORg5222 OR saphris OR sycrest OR batelapine OR "cgs 13429" OR cgs13429 OR belaperidone OR balaperidone OR "lu 111995" OR lu111995 OR bifeprunox OR "du 127090" OR du127090 OR emonapride OR emirace OR nemonapride OR "ym 09151" OR "ym 09151 02" OR "ym 09151 2" OR "ym 09151-02" OR "ym 09151-2" OR ym09151 OR "ym09151 02" OR "ym09151 2" OR "ym09151-02" OR "ym09151-2" OR ym0915102 OR ym091512 OR elopiprazole OR flumezapine OR "ly 120363" OR ly120363 OR fluoxetine OR symbya OR hp873 OR "ilo 522" OR ilo522 OR zomaril OR lurasidone OR latuda OR "mk 3756" OR mk3756 OR "sm 13496" OR sm13496 OR "smp 13496" OR smp13496 OR melperone OR bunil OR buronil OR eunerpan OR "fg 5111" OR fg5111 OR flubuperone OR melperon OR methylperone OR metylperone OR metylperonum OR "sdz 208 912" OR "sdz 208-912" OR "sdz 208912" OR "sdz 912" OR "sdz hdc 912" OR "sdz hdc912" OR "sdz208 912" OR "sdz208-912" OR sdz208912 OR sdz912 OR "sdz 208 911" OR "sdz 208-911" OR "sdz 208911" OR "sdz 911" OR "sdz hac 911" OR "sdz hac911" OR "sdz208 911" OR "sdz208-911" OR sdz208911 OR sdz911 OR "fg 5803" OR fg5803 OR nORclozapine OR demethylclozapine OR desmethylclozapine OR ocaperidone OR "r 79598" OR r79598 OR olanzapine OR anzatric OR "dopin tab" OR "jolyon md" OR lanopin OR lanzac OR "ly 170053" OR ly170053 OR meltolan OR midax OR olace OR oladay OR olan OR olandus OR olanex OR olansek OR olapin OR olazax OR oleanz OR olexar OR oltal OR olzap OR onza OR "ozapin md" OR

psychozap OR relprev OR zalasta OR zelta OR zydis OR zypadhera OR zyprex OR zyprexa OR zyprexav OR paliperidone OR invega  
 OR "paliperidone palmitate" OR "r 76477" OR r76477 OR "ro 76477" OR "ro 92670" OR ro76477 OR ro92670 OR xelion OR  
 panamesine OR "emd 57445" OR emd57445 OR pentiapine OR "cgs 10746" OR cgs10746 OR "cgs 10746b" OR cgs10746b OR  
 perlapine OR "aw 14'2333" OR "aw 142333" OR aw142333 OR perlapin OR perospirone OR lullan OR "sm 9018" OR sm9018  
 OR pridopidine OR "acr 16" OR acr16 OR "asp 2314" OR asp2314 OR "fr 310826" OR fr310826 OR huntexil OR quetiapine OR  
 "ici 204636" OR "ici 204646" OR ici204636 OR ici204646 OR seroquel OR socalm OR tienapine OR remoxipride OR "a 33547"  
 OR a33547 OR "fla 731" OR fla731 OR roxiam OR rilapine OR sertindole OR "lu 23174" OR lu23174 OR "s 1991" OR s1991  
 OR serdolect OR serlect OR sulpiride OR abilit OR aiglonyl OR arminol OR dobren OR dogmatil OR dogmatyl OR dolmatil OR  
 eglonyl OR equilid OR "fk 880" OR fk880 OR isnamide OR levobren OR levopraid OR levosulpiride OR meresa OR miradol OR  
 neogama OR sulfiride OR sulpivert OR sulpyride OR synedil OR vipral OR sultopride OR barnetil OR barnotil OR "ms 5024" OR  
 ms5024 OR sulfopride OR tenilapine OR tiopirone OR "bmy 13859" OR bmy13859 OR "mj 13859" OR "mj 13859 1" OR "mj  
 13859-1" OR mj13859 OR "mj13859 1" OR "mj13859-1" OR mj138591 OR tiapirone OR volinanserine OR "m 100907" OR  
 m100907 OR "mdl 100151" OR "mdl 100907" OR mdl100151 OR mdl100907 OR ziprasidone OR "cp 88059" OR "cp 88059  
 01" OR "cp 88059 27" OR "cp 88059-01" OR "cp 88059-27" OR "cp 8805901" OR "cp 8805927" OR cp88059 OR "cp88059  
 01" OR "cp88059 27" OR "cp88059-01" OR "cp88059-27" OR cp8805901 OR cp8805927 OR geodon OR zeldox OR zeldrox OR  
 zipsydon OR zotepine OR lodopin OR nipolept OR azaperone OR "r-1929" OR r1929 OR sedaperone OR stresnil OR benperidol  
 OR anquil OR benperidone OR benzoperidol OR benzperidol OR benperidolneuraxpharm OR "cb 8089" OR cb8089 OR frenactyl  
 OR frenactil OR glianimon OR "mcn jr 4584" OR "mcn jr4584" OR phenactil OR "r 4584" OR r4584 OR berupipam OR "nnc  
 22 0010" OR "nnc22 0010" OR bitopertin OR paliflutine OR "r 1678" OR r1678 OR "rg 1678" OR rg1678 OR "ro 4917838"  
 OR ro4917838 OR blonanserine OR "ad 5423" OR ad5423 OR lonasen OR brexpiprazole OR "opc 34712" OR opc34712 OR  
 brofexine OR dimetabrone OR "fi 6820" OR fi6820 OR bromospiperone OR bromospiroperidol OR bromperidol OR impromen  
 OR "r 11,333" OR "r 11333" OR "r11,333" OR r11333 OR tesoprel OR "impromen decanoate" OR "r 46,541" OR "r 46541" OR  
 "r46,541" OR r46541)  
 #20 #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4  
 OR #3 OR #2 OR #1  
 #21 TS=(Confusion OR Confused OR Delirium OR Delirious OR (Psychomotor W2 Agitat\*) OR Hallucinat\* OR (Charles W2  
 Bonnet W2 Syndrome) OR Illusion\* OR Delusion\* OR Paranoi\* OR Dementia\* OR Amnes\* OR Cognit\* OR Psychotic OR psychosis)  
 #22 TS=(inattention OR inattentive\* OR "icu syndrome" OR (intensive W2 care W2 syndrome) OR "acute brain dysfunction" OR  
 (acute W2 brain W2 dysfunction\*) OR "septic encephalopath\*" OR "acute brain failure" OR "acute organic psychosyndrome\*" OR  
 "acute brain syndrome" OR "metabolic encephalopath\*" OR "acute psycho-organic syndrome\*" OR "clouded state" OR "clouding of  
 consciousness" OR "exogenous psychosis" OR "toxi psychosis" OR "icu psychosis")  
 #23 (TS=(brain W3 disease\*) ) AND (TS=(((Catastrophic OR Critical) W2 Illness\*) OR "Critically Ill" OR Sepsis OR Septic))  
 #24 (TS=(brain W3 disease\*) ) AND (TS=(((Intensive OR Critical\* OR coronary\* OR Respiratory OR Stroke) W2 Care W2 Unit\*)  
 OR ICU OR CCU))  
 #25 (TS=(brain W3 disease\*) ) AND (TS=(Hospitaliz\* OR Hospitalis\* OR "Length of Stay" OR LOS OR (Patient\* W2 Admission\*)  
 OR (Patient\* W2 Discharge\*) OR Readmission OR Readmitt\*))  
 #26 #25 OR #24 OR #23 OR #22 OR #21  
 #27 #20 AND #26  
 #28 TS=(((clinical OR random\* OR Control\*) W2 trial\*) OR RCT\* OR CCT\*)  
 #29 #27 AND #28

## Appendix 6. World Health Organization LILACS Search Strategy

Database: World Health Organization LILACS (1986 to July 20, 2017)

Search Strategy:

tw:(antipsychotic agents OR acepromazine OR acetopromazine OR vetranquil OR acetylpromazine OR acepromazine OR calmivet  
 OR acetazine OR notensil OR plegicil OR promace OR soprintin OR anatron OR anergan OR atravet OR "cb 1522" OR cb1522 OR  
 plegicin OR plegicyl OR sedalin OR soprintin) AND (instance:"regional") AND (db:"LILACS") AND type of study:( "clinical trials"  
 OR "guideline")



## Appendix 7. Database of Abstracts of Reviews of Effects Search Strategy

Database: Database of Abstracts of Reviews of Effects (2nd quarter of 2017)

Search Strategy:

1 Antipsychotic drugs/ or Antipsychotic Agent/(antipsychotic\* or neuroleptic\* or (major adj2 (tranquilizer\* or tranquiliser\*))).mp.  
 2 aceperone/ or (aceperone or acetabutone or acetobutone or "r 3248" or r3248).mp.  
 3 Acepromazine/ or acepromazine maleate/ or (acepromazine or acetopromazine or vetranquil or acetylpromazine or acepromazine or calmivet or acetazine or notensil or plegicil or promace or soprintin or anatron or anergan or atravet or "cb 1522" or cb1522 or plegicin or plegicil or sedalin or soprintin).mp.  
 4 aceprometazine/ or (aceprometazine or acepromethazine or acetylpromethazine).mp.  
 5 acetophenazine / or (acetophenazine or acephenazine or "nsc 70600" or nsc70600 or "sch 6673" or sch6673 or tindal).mp.  
 6 adopraine / or (adopraine or adopratin or "slv 313" or slv313).mp.  
 7 alimemazine/ or (alimemazin or alimemasine or alimemazin\* or alimezine or "bayer 1219" or electrotrimeprazine or methylpromazine or palpex or "rp 6549" or rp6549 or trimeprazine or trimeprezine or varialgil or nedeltran or panectyl or repeltin or temaril or temaryl or teralen or teralene or theralen or theralene or valergan or vallergeran).mp.  
 8 "alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol"/ or ("bms 181100" or bms181100 or "bmy 14802" or "bmy 14802 1" or "bmy 14802-1" or bmy14802 or "bmy14802 1" or "bmy14802-1" or bmy148021).mp.  
 9 "alpha [1 [2 (1,4 benzodioxan 5 yloxy)ethyl] 3 pyrrolidinyl] 4 fluoroacetophenone"/ or ("s 16924" or s16924).mp.  
 10 amitriptyline plus perphenazine/ or amitriptyline perphenazine/ or (amitriptyline or ((amitriptyline adj2 perphenazine) or "anxiress-d" or "duo-vil 2-10" or "duo-vil 2-25" or "duo-vil 4-10" or etrafon or etraphon or longopax or mutabon or mutanxion or mutaspline or "neuragon-a" or "neuragon-b" or pertriptyl or polybon or triavil or triptafen)).mp.  
 11 aplindore/ or (aplindore or "dab 452" or dab452 or palindore or "way dab 452" or "way dab452").mp.)  
 12 atypical antipsychotic agent/ or "1 cyclopropylmethyl 4 [2 (4 fluorophenyl) 2 oxoethyl]piperidine"/ or "1,2,3,4,8,9,10,10a octahydro 7bh cyclopenta[b][1,4]diazepino[6,7,1 hi]indole"/ or "2 amino n [4 [4 (1,2 benzisothiazol 3 yl) 1 piperazinyl]butyl]benzamide"/ or "2 chloro 11 (3 dimethylaminopropylidene)morphanthridine"/ or "4 (4 fluorophenyl) 1,2,3,6 tetrahydro 1 [4 (1,2,4 triazol 1 yl)butyl]pyridine"/ or "4,9 dibromo 6 (4 methyl 1 piperazinyl)benzo[b]pyrrolo[3,2,1 jk][1,4]benzodiazepine"/ or "7 [3 [4 (2,3 dimethylphenyl) 1 piperazinyl]propoxy] 2(1h) quinolinone"/ or "7 chloro 2 [[1 (2 methoxyphenyl) 4 piperidyl]methylaminomethyl] 1,4 benzodioxan"/ or "8 fluoro 4 [3 (2 methoxyethyl) 4 methyl 1 piperazinyl] 2 methyl 10h thieno[2,3 b][1,5]benzodiazepine"/ or atypical antipsychotic agent/ or (atypical adj2 (antipsychotic\* or neuroleptic\*)).mp. or abaperidone/ or (abaperidone or "fi 8602" or fi8602).mp. or alentamol/ or (alentamol or alentemol or "u 66444b" or "u 68552b" or "u 68553b" or u66444b or u68552b or u68553b).mp. or amisulpride/ or (aminosultopride or amisulpride or amisulpridum or "dan 2163" or dan2163 or sertol or socian or solian).mp. or amperozide/ or (amperozide or "fg 5606" or fg5606).mp. or aripiprazole/ or (aripiprazole or abilify or abilitat or "opc 14597" or opc14597).mp. or asenapine/ or (asenapine or "org 5222" or org5222 or saphris or sycrest).mp. or batelapine/ or (batelapine or "cgs 13429" or cgs13429).mp. or belaperidone/ or (belaperidone or balaperidone or "lu 111995" or lu111995).mp. or bifeprunox/ or (bifeprunox or "du 127090" or du127090).mp. or elopiprazole/ or emonapride/ or (emonapride or emirace or nemonapride or "ym 09151" or "ym 09151 02" or "ym 09151 2" or "ym 09151-02" or "ym 09151-2" or ym09151 or "ym09151 02" or "ym09151 2" or "ym09151-02" or "ym09151-2" or ym0915102 or ym091512).mp. or flumetazapine/ or (flumetazapine or "ly 120363" or ly120363).mp. or fluoxetine plus olanzapine/ or ((fluoxetine adj2 olanzapine) or symbyax).mp. or fluperlapine/ or (fluperlapine or "nb 106689" or nb106689).mp. or iloperidone/ or (iloperidone or fanapt or fanaptum or "hp 873" or hp873 or "ilo 522" or ilo522 or zomaril).mp. or lurasidone/ or (lurasidone or latuda or "mk 3756" or mk3756 or "sm 13496" or sm13496 or "smp 13496" or smp13496).mp. or melperone/ or (melperone or bunil or buronil or eunerpan or "fg 5111" or fg5111 or flubuperone or melperon or methylperone or metylperone or metylperonum).mp. or "n (2 chloro 6 methylergolin 8alpha yl)pivalamide"/ or ("sdz 208 912" or "sdz 208-912" or "sdz 208912" or "sdz 912" or "sdz hdc 912" or "sdz hdc912" or "sdz208 912" or "sdz208-912" or sdz208912 or sdz912).mp. or "n (2,6 dimethylergolin 8alpha yl)pivalamide"/ or ("sdz 208 911" or "sdz 208-911" or "sdz 208911" or "sdz 911" or "sdz hac 911" or "sdz hac911" or "sdz208 911" or "sdz208-911" or sdz208911 or sdz911).mp. or "n cyclohexyl 4 [4 (4 fluorophenyl) 4 oxobutyl] 1 piperazinecarboxamide"/ or ("fg 5803" or fg5803).mp. or norclozapine/ or (norclozapine or demethylclozapine or desmethylclozapine).mp. or ocaperidone/ or (ocaperidone or "r 79598" or r79598).mp. or olanzapine/ or (olanzapine or anzatic or "dopin tab" or "jolyon md" or lanopin or lanzac or "ly 170053" or ly170053 or miltolan or midax or olace or oladay or olan or olandus or olanex or olansek or olapin or olazax or oleanz or olexar or olta or olzap or onza or "ozapin md" or psychozap or relprev or zalasta or zelta or zydis or zypadhera or zyprex or zyprexa or zyprexav).mp. or paliperidone/ or (paliperidone or invega or "paliperidone palmitate" or "r 76477" or r76477 or "ro 76477" or "ro 92670" or ro76477 or ro92670 or xeplion).mp. or panamazine/ or (panamazine or "emd 57445" or emd57445).mp. or pentiapipe/ or pentiapipe maleate/ or (pentapipe or "cgs 10746" or cgs10746 or "cgs 10746b" or cgs10746b).mp. or perlapine/ or (perlapine or "aw 14'2333" or "aw 142333" or aw142333 or perlapin).mp. or perospirone/ or

(perospirone or lullan or "sm 9018" or sm9018).mp. or pridopidine/ or (pridopidine or "acr 16" or acr16 or "asp 2314" or asp2314 or "fr 310826" or fr310826 or huntexil).mp. or quetiapine/ or (quetiapine or "ici 204636" or "ici 204646" or ici204636 or ici204646 or seroquel or socalm or tienapine).mp. or remoxipride/ or (remoxipride or "a 33547" or a33547 or "fla 731" or fla731 or roxiam).mp. or rilapine/ or rilapine.m.p. or sertindole/ or (sertindole or "lu 23174" or lu23174 or "s 1991" or s1991 or serdolect or serlect).mp. or sulpiride/ or (sulpiride or abilit or aiglonyl or arminol or dobren or dogmatil or dogmatyl or dolmatil or eglonyl or equilid or "fk 880 " or fk880 or isnamide or levobren or levopraid or levosulpiride or meresa or miradol or neogama or sulfiride or sulpivot or sulpyride or synedil or vipral).mp. or sultopride/ or (sultopride or barnetil or barnotil or "ms 5024" or ms5024 or sulfopride).mp. or tenilapine/ or tenilapine.m.p. or tiospirone/ or (tiospirone or "bmy 13859" or bmy13859 or "mj 13859" or "mj 13859 1" or "mj 13859-1" or mj13859 or "mj13859 1" or "mj13859-1" or mj138591 or tiaspirone).mp. or volinanserine/ or (volinanserine or "m 100907" or m100907 or "mdl 100151" or "mdl 100907" or mdl100151 or mdl100907).mp. or ziprasidone/ or (ziprasidone or "cp 88059" or "cp 88059 01" or "cp 88059 27" or "cp 88059-01" or "cp 88059-27" or "cp 8805901" or "cp 8805927" or cp88059 or "cp88059 01" or "cp88059 27" or "cp88059-01" or "cp88059-27" or cp8805901 or cp8805927 or geodon or zeldox or zeldrox or zipsydon).mp. or zotepine/ or (zotepine or lodopin or nipolept).mp.

13 Azaperone/ or (azaperone or "r-1929" or r1929 or sedaperone or stresnil).mp.)

14 Benperidol/ or (benperidol or anquil or benperidone or benzoperidol or benzperidol or benperidolneuraxpharm or "cb 8089" or cb8089 or frenactyl or frenactil or glianimon or "mcn jr 4584" or "mcn jr4584" or phenactil or "r 4584" or r4584).mp.

15 berupipam/ or (berupipam or "nnc 22 0010" or "nnc22 0010").mp.

16 bitopertin/ or (bitopertin or paliflutine or "r 1678" or r1678 or "rg 1678" or rg1678 or "ro 4917838" or ro4917838).mp.

17 blonanserine/ or (blonanserine or "ad 5423" or ad5423 or lonasen).mp.

18 brexpiprazole or (brexpiprazole or "opc 34712" or opc34712).mp.

19 brofexine/ or (brofexine or dimetabrone or "fi 6820" or fi6820).mp.

20 bromospiperone/ or (bromospiperone or bromospiroperidol).mp. (0)

21 bromperidol/ or bromperidol decanoate/ or (bromperidol or impromen or "r 11,333" or "r 11333" or "r11,333" or r11333 or tesoprel or "impromen decanoate" or "r 46,541" or "r 46541" or "r46,541" or r46541).mp.

22 Butaclamol/ or Dibenzocycloheptenes/ or ("ay 23,028" or "ay 23028" or "ay23,028" or "ay-23028" or ay23028 or butaclamol).mp.

23 butaperazine/ or (butaperazine or "ahr 3000" or "bayer 1362" or butaperazinum or butyrylperazin or butyrylperazine or megalectil or randolectil or randolectyl or repoise or "riker 595" or tyrylen).mp.

24 carfenazine/ or (carfenazine or carfenazinum or carphenazine or "nsc 71755" or nsc71755 or procethazine or proketazine or "wy 2445" or wy2445).mp.

25 cariprazine/ or (cariprazine or "mp 214" or mp214 or "rgh 188" or rgh188).mp.

26 carpipramine/ or (carpipramine or carbadipimidine or defecton or defekton or prazinil or "pz 1511" or pz1511 or "rp 21679" or rp21679).mp.

27 carvotroline/ or (carvotroline or "wy 47791" or wy47791).mp.

28 centbutindole/ or centbutindole.m.p.

29 chlorothiazide plus reserpine/ or (chlorothiazide or "diupres-250" or "diupres-500").mp.

30 chlorphenethazine/ or (chlorphenethazine or chlorfenethazine or elroquil or marophen).mp.

31 chlorproethazine/ or (chlorproethazine or neuriplege or "rp 4909" or rp4909).mp.

32 chlorpromazine/ or chlorpromazine plus dexamphetamine/ or chlorpromazine sulfoxide/ or (chlorpromazine or "2601 a" or "4560 r p" or aminasin or aminasine or aminazin or aminazine or ampliactil or ampticil or ancholactil or aspersinal or bellacina or cepezet or chlomazine or "chlor pz" or chloractil or chlorazine or chlorbromasin or chlorderazine or chlorderazin or chlormazine or chlorpromanyl or chlorpromazin or chlorpromed or clonazine or clordelazin or clorpromaz or clorpromazine or clozine or contomin or duncan or elmarin or esmino or fenactil or hibanil or hibernal or hibernal or "hl 3746" or "hl 5746" or klorproman or klorpromazin or klorpromex or laractyl or largactil or largactyl or matcine or megaphen or megatil or "ml 5746" or neomazine or neurazine or novomazina or phenathyl or plegomazin or plegomazine or proma or promacid or promactil or promapar or promazil or promexin or propaphen or propaphenin or prozil or prozin or psychozine or psynor or "rp 4560" or sanopron or "skf 2601 a" or solidon or sonazine or taroctil or taroctyl or "thor prom" or thorazene or thorazine or torazina or "vegetamin a" or "vegetamin b" or winsumin or wintamine or wintermin or zuledin or "thora-dex" or opromazine or secotil).mp.

33 Chlorprothixene/ or (chlorprothixene or chloprothixene or "chlor prothixene" or chlorprothixene or chlorprothixen or chlorprothixenechloride or chlorprotixen or chlorprotixene or chlothixen or "n 714" or "n 7714" or "ro 4 0403" or "ro 40403" or taractan or tarasan or traquilan or troxen or truxal or truxaleta or truxaletten).mp.

34 cinuperone/ (cinuperone or "hr 375" or hr375).mp.

35 clocapramine/ or (clocapramine or "y 4153" or y4153).mp.

36 cloflumide mesilate/ or ("cloflumide mesylate" or "vufb 15496" or vufb15496).mp.

37 clofluperol/ or (clofluperol or seperidol).mp.

38 clopenthixol/ or or THIOXANTHENES/ or TRANQUILIZING AGENTS/ or clopenthixol decanoate/ or (clopenthixol or “ay 62021” or ay62021 or chlorpenthixol or chlorperphenthixene or chlorperphenthixene or ciatyl or cisordinol or clopenthixol or cloxipol or “n 746” or n746 or “nsc 64087” or nsc64087 or sordinol or zuclopenthixol).mp.

39 clopimozide/ or (clopimozide or “r 29,764” or “r 29764” or “r29,764” or r29764).mp.

40 clpipazan/ or (clpipazan or “skf 69634” or skf69634).mp.

41 cospipramine/ or (cospipramine or cremin or mosapramine or “y 516” or y516).mp.

42 clotiapine/ or (clotiapine or clothiapien or clothiapien or entumin or entumine or etumine or “hf 2159” or hf2159).mp.

43 cp 903397/ or (“cp 903397” or cp903397).mp.

44 cryptenamine plus reserpine/ or (cryptenamine or “unitensen-r”).mp.

45 Clozapine/ or Dibenzazepines/ or Piperazines/ or clozapine derivative/ or clozapine n oxide/ or (alemoxan or azaleptin or clopine or clapsine or clozapin\* or clozaril or denzapine or dorval o rdozapine or elcrit or fazaclo or “hf 1854” or hf1854 or lapenax or leponex or lozapin\* or sizopin or versacloz or “wander compound” or zapen or zaponex).mp.

46 cyamemazine/ or (cyamemazine or cianatil or cyamepromazine or “fi 6229” or fi6229 or kyamepromazin or “rp 7204” or rp7204 or tercián).mp.

47 dexamphetamine plus prochlorperazine/ or ((dextroamphetamine adj2 sulfate adj2 prochlorperazine) or “eskatrol spansule”).mp.

48 dexamphetamine plus reserpine/ or ((dexamphetamine or dexserpine or dextroamphetamine) adj2 reserpine).mp.

49 diethylstilbestrol plus methyltestosterone plus reserpine/ or ((diethylstilbestrol adj2 methyltestosterone) or tylandril).mp.

50 dimetotiazine/ or (dimetotiazine or banistyl or dimethiotiazine or dimethiothazine or dimethothiazine or dimethotiazine ro dime-tiotiazine or fonazine or “il 6302”).mp.

51 dimevamide plus phenobarbital plus reserpine/ or ((dimevamide adj2 phenobarbital) or “neuro-centrine tablet\*”).mp.

52 dixyrazine/ or (dixyrazine or dixirazine or dixyrazin or dyxirazine or esocalm or esucos or metronal or roscal or “ucb 3412” or ucb3412).mp.

53 dolasetron mesilate/ or (dolasetron or anemet or anzemet or “mdl 73147” or “mdl 73147ef” or mdl73147 or mdl73147ef or zamanon).mp.

54 Droperidol/ or or droperidol plus fentanyl/ or droperidol plus fentanyl citrate/ or (droperidol or dehidrobenzoperidol or dehydrobenzoperidol or dehydrobenzoperiol or dehydrobenzperidol or dehydrobenzperidolum or dridol or droleptan or droperol or halkan or inaprine or inapsin or inapsine or “mcn jr 4749” or “mcn r 4749” or oridol or “r 4749” or sintodian or troperidol or xomolix or innovan or innovar or inoval or inovar or talamonal or thalamonal or disifelit).mp.

55 duoperone/ or (duoperone or “ahr 6646” or ahr6646).mp.

56 ephedrine sulfate plus reserpine/ or ((ephedrine adj2 sulfate) or renir).mp.

57 ethinylestradiol plus reserpine/ or ((ethinylestradiol adj2 reserpine) or estrosed or sergynol).mp.

58 etymemazine/ or (etymemazine or diquel or ethotrimprazine or ethylisobutrazine or ethymemazine or nuital or “rp 6484” or rp6484 or sergetyl).mp.

59 Etazolate/ or Pyridines/ or (etazolate or sq20009 or “sq-20009” or “sq 20009”).mp.

60 farampator/ or (farampator or “cx 691” or cx691 or “org 24448” or org24448).mp.

61 fluanisone/ or (fluanisone or “anti pica” or antipica or fluanisone\* or fluанизone or fluoanisone or haloanisone or haloanisone or “md 2028” or md2028 or “r 2028” or “r 2167” or r2028 or r2167 or sedalande or sedalanide or solusediv).mp.

62 Flupenthixol/ or flupenthixol decanoate/ or (flupenthixol or flupenthixol\* or emergil or fluaxol or fluxanxol or “lc 44” or lc44 or “n 7009” or n7009 or siplaryl or siplaryl or depixol or depot or “lu 5 110” or “lu 5110” or viscoleo).mp.

63 Fluphenazine/ or fluphenazine decanoate/ or fluphenazine enanthate/ or (fluphenazin\* or anatensil or anatensol or antasol or cenilene or dapotum or elinol or flufenan or flufenazine or flumezin or fluorfenazine or fluphenacin or “fluzine-p” or ftorphenazine or “luogen depot” or lyogen or lyorodin or moditen or moditin or omca or pacinol or permitil or phthorphenazine or potensone or prolixan or prolixene or prolixin\* or “s 94” or sevinol or sevinol or squaline or squalone\* or siquoline or “sq 4918” or sq4918 or tensofin or trancin or valamina or vespazin\* or “dapatum d25” or dapotum or decafen or flucan or fludecasine or fludecate or lyogen or mirenil or modocate or phlufdek or sydepres or flunanthate).mp.

64 Fluspirilene/ or (fluspirilene or fluspi or fluspirilen or imap or “mcn jr 6218” or “mcn jr6218” or “r 6218” or r6218 or redeptin or spirodiflamine or kivat).mp.

65 flutroline/ or (flutroline or “cp 36,584” or “cp 36584” or “cp36,584” or cp36584).mp.

66 “gamma endorphin[deenkaphalin]”/ or ((endorphin adj2 deenkaphalin) or “beta endorphin[6-17]” or “beta lipotropin[66-77]” or “org 5878” or org5878).mp.

67 gevetroline/ or (gevetroline or “wy 47384” or wy47384).mp.

68 glyceryl trinitrate plus pentaerythryl tetranitrate plus reserpine/ or penite).mp.

69 Haloperidol/ or haloperidol decanoate/ or (haloperidol or alased or aloperidin\* or avant or binison or brotopon or celenase or cereen or cerenace or cizoren or depidol or dores or dozic or duraperidol or "einalon s" or fortunat or govotil or haldol or halidol or "halo-p" or halojust or halomed or haloneural or haloper or haloperil or haloperin or haloperitol or halopidol or halopol or halosten or haricon or "haridol-d" or keselan or linton or "lodomer-2" or "mcn jr 1625" or "mcn jr1625" or mixidol or novoperidol or "nsc 170973" or nsc170973 or peluces or perida or peridol or peridor or "r 1625" or r1625 or selezyme or seranace or serenace or serenase or serenelfi or siegoperidol or sigaperidol or trancodol or pericate or "r 13,672" or "r 13672" or senorm).mp.

70 hexamethonium chloride plus reserpine/ or (hexamethonium or reserthonium).mp.

71 hydralazine plus reserpine/ or hydrochlorothiazide plus potassium chloride plus reserpine/ or hydrochlorothiazide plus reserpine/ or (dralserp or (hydralazine adj2 reserpine) or "serpasil-apresoline" or "hydropresor dichlotride s" or "h.r.-50" or "hydro-reserp" or hydrochlorothiazide or hydroserpine or "medeserpine co" or "serpasil-esidrix").mp.

72 hydrochlorothiazide plus reserpine plus secbutabarbita/ or ((hydrochlorothiazide adj2 reserpine adj2 secbutabarbita) or butiserpazide).mp.

73 hydroflumethiazide plus potassium chloride plus reserpine/ or ((hydroflumethiazide adj4 reserpine) or rautrax).mp.

74 hydroflumethiazide plus reserpine/ or ((hydroflumethiazide adj2 reserpine) or salutensin\*).mp.

75 isofloxythepin/ or (isofloxythepin or "vufb 10662").mp.

76 isomolpan/ or (isomolpan or "cgs 15855" or "cgs 15855 a" or "cgs 15855a" or cgs15855 or cgs15855a).mp.

77 isopropamide iodide plus prochlorperazine maleate/ or ((isopropamide adj4 prochlorperazine) or "combid spansule").mp.

78 lenperone/ or (lenperone or "ahr 2277" or ahr2277 or elanone).mp.

79 levomepromazine/ or (levomepromazine or "apo-methoprazine" or "bayer 1213" or "cl 36467" or "cl 39743" or cl36467 or cl39743 or hiranamin or mepromazine or levium or promazine or levomeprazine or levopromazin\* or levoprome or levozin or mepromazine or methotrimprazine or methozane or milezin or minozinan or neozine or neuractil or neurocil or nirvan or nozinan or "rp 7044" or rp7044 or sinogan or "sk and f 5116" or "skf 5116" or skf5116 or tiscerin or tiscerin or veractil).mp.

80 lithium/ or lithium.mp.

81 Loxapine/ or loxapine succinate/ or (loxapine or adasuve or "alxz 004" or alxz004 or "az 004" or az004 or "cl 62,362" or "cl 62362" or "cl62,362" or cl62362 or "cl 71563" or "cl-71563" or cl71563 or loxapinsuccinate or cloxazepin\* or loxapane or loxapin\* or loxitane or oxilapine or "sum 3170" or sum3170 or daxolin or desconex or loxapac).mp.

82 maroxepine/ or maroxepine.mp.

83 mazapertine/ or (mazapertine or "rwj 37796" or rwj37796).mp.

84 mepiprazole/ or meprobamate plus promazine/ or (mepiprazole or "emd 16923" or emd16923 or psigodal or prozine or meproba-mate).mp.

85 Mesoridazine/ or Phenothiazines/ or Tranquilizing Agents/ or mesoridazine besylate/ or (mesoridazin\* or esoridazine or lidanar or lidanil or mesorin or "nc 123" or (thioridazine adj2 sulfoxide) or "tps 23" or serentil).mp.

86 methamphetamine plus reserpine/ or ((methamphetamine adj2 reserpine) or "du-oria").mp.

87 Methiothepin/ or Dibenzothiepins/ or Piperazines/ or methyclothiazide plus reserpine/ or (methiothepin\* or metitepine).mp.

88 methopromazine/ or (methopromazine or methoxypropazine or metopromazine or "diutensen-r").mp.

89 Methotrimprazine/ or (levopromazine or tizercine or methotrimprazine or levomepromazine or levomeprazin or tiscerin or tizertsin).mp.

90 metofenazate/ or (metofenazate or frenolon or metaphenazine or methophenazine or metophenazine or phrenolon).mp.

91 Molindone/ or indoles/ or (molindon\* or "en 1733a" or en1733a or lidone or moban or molindor).mp.

92 moperone/ or (moperone or luvatrene or luvatrene or "methyl peridol" or methylperidol\* or moperon or "r 1658").mp.

93 "n [(1 butyl 2 pyrrolidinyl)methyl] 2,3 dihydro 2 methyl 5 sulfamoyl 7 benzofurancarboxamide"/ or ("y 20024" or y20024).mp.

94 "n [3 (4 fluorophenyl) 3 (4 phenylphenoxy)propyl]sarcosine"/ or ("alx 5407" or alx5407 or NFPS).mp.

95 "n [4 [2 (6 cyano 1,2,3,4 tetrahydro 2 isoquinolinyl)ethyl]cyclohexyl] 4 quinolinecarboxamide"/ or ("sb 277011" or "sb 277011a" or sb277011 or sb277011a).mp.

96 neboglamine/ or (neboglamine or "cr 2249" or cr2249 or "xy 2401" or xy2401).mp.

97 nicotinic acid plus pentetrazole plus reserpine/ or ((nicotinic adj4 pentetrazole adj4 reserpine) or (nicozol adj2 reserpine)).mp.

98 noctran/ or noctran.mp.

99 norchlorpromazine/ or (norchlorpromazine or demethylchlorpromazine or demonomethylchlorpromazine or desmethylchlorpromazine or desmonomethylchlorpromazine or monodesmethylchlorpromazine).mp.

100 Ondansetron/ or Imidazoles/ or (ondansetron or gr38032f or "gr 38032f" or "sn 307" or sn307 or "gr-38032f" or "sn-307" or zofran).mp.

101 oxiperomide/ or (oxiperomide or "r 4714" or r4714).mp.

- 102 oxypertine/ or (oxypertin\* or “cl 77328” or cl77328 or equipertine or forit or opertil or oxipertin or oxypertin or “win 18501 2” or “win 18501-2” or “win 185012” or “win18501 2” or “win18501-2” or win185012).mp.
- 103 oxyprothepine/ or oxyprothepine decanoate/ or (oxyprothepine or oxyprothepin).mp.
- 104 pecazine/ or (pecazine or lacumin or mepasin or mepazine or nothiazine or “p 391” or pacatal or pacatol or pactal or papital or paxital or pecazine or “w 1224”).mp.
- 105 Penfluridol/ or (penfluridol or “mcn jr 16,341” or “mcn jr 16341” or micefal or “r 16,341” or “r 16341” or semap or “r 16341” or “r-16341” or r16341).mp.
- 106 Perazine/ or (perazine or taxilan).mp.
- 107 pentaerythrityl tetranitrate plus reserpine/ or pentaerythrityl tetranitrate plus reserpine plus secbutabarbital/ or (pentaerythrityl or pentaserpine or respet or pentraline).mp.
- 108 pentobarbital plus reserpine/ or (“nambu-serpine” or (pentobarbital adj2 reserpine)).mp.
- 109 perazine/ or (perazine or “p 725” or pernazine or taxilan).mp.
- 110 periciazine/ or (periciazine or aolept or neulactil or neuleptil\* or periciazinum or pericyazine or propericiazine or propericiazin or propericiazine or “rp 8909” or “skf 20716”).mp.
- 111 perimetazine/ or (perimetazine or “1317 an” or “an 1317” or an1317 or leptyl or perimethazine).mp.
- 112 Perphenazine/ or perphenazine decanoate/ or perphenazine enanthate.mp. or (perphenazine or chlorperphenazine or chlorpiprazine or chlorpiprozine or decentan or etaperazine or ethaperazine or “f-mon” or fentazin or leptopsique or peratsin or perfenazine or perforazine or pernamed or perphenan or perphenazin\* or “perzine-p” or porazine or “sch 3940” or thilatazin or tranquisan or trifalon or trilafan or trilafon or trilifan or triliphan or triomin).mp.
- 113 (“pf 217830” or pf217830 or “pf 2400013” or pf2400013 or “pf 3463275” or pf3463275).mp.
- 114 phenobarbital plus reserpine/ or phenobarbital plus reserpine plus theobromine/ or phenobarbital plus reserpine plus thiamine.mp. or ((phenobarbital adj2 reserpine) or “solfo-serpine” or bromoserpin or “theo-serp” or “theobarb-r” or theoserpin or besertal or “neo-slowten”).mp.
- 115 picobenzide/ or (picobenzide or dosetil or “m 14012 4” or “ma 14012” or picobenzamide).mp.
- 116 piflutixol/ or piflutixol.mp.
- 117 pimavanserine/ or (pimavanserine or “acp 103” or acp103).mp.
- 118 pimethixene/ or (pimethixene or “bp 400” or “bp 400 e” or “bp 400e” or bp400 or bp400e or muricalm or pimetixin).mp.
- 119 Pimozide/ or (pimozide or antalon or “mcn jr 6238” or opiran or orap or pimocide or pimoride or pinozide or pizide or “r 6238” or r6238).mp.
- 120 pipamperone/ or (pipamperone or dipeperon or dipiperon or “dl piperonyl” or floropipamide or “piperonyl of pripamperone of r 3345” or r3345).mp.
- 121 piperacetazine/ or (piperacetazine or “pc 1421or pc1421” or quide).mp.
- 122 pipotiazine/ or pipotiazine palmitate/ or pipotiazine undecenoate/ or (pipotiazine or “9366 rp” or piportil or pipothiazine or “rp 19366” or rp19366 or “il 19552” or il19552 or “rp 19552” or rp19552 or rp 19551).mp.
- 123 pirenperone/ or polythiazide plus reserpine/ or (pirenperone or “r 47,465” or “r 47465” or “r 50656” or “r47,465” or r47465 or r50656 or “renese r” or “renese-r”).mp.
- 124 pomaglumetad methionil/ or (“pomaglumetad methionil” or “ly 2140023” or ly2140023).mp.
- 125 Prochlorperazine/ or prochlorperazine edisylate/ or prochlorperazine maleate/ or (compazine or prochlorperazine or “6140 rp” or antinaus or “bayer a 173” or “bayer 173” or capazine or chlormepazine or chlorpeazine or chlorperazine or compro or dicopal or emelent or klometil or kronocin or meterazine or metherazine or nautisol or nipodal or normalmin or pasotomin or prochlor or prochlorpemazine or prochlorperacine or prochlorperzine or prochlorpromazine or prochlorperazine or procot or “rp 6140 ir rp6140” or “sk and f 4657” or “skf 4657” or skf4657 or tementil or temetil or buccastem or dhaperazine or emeteral or emetiral or nibromin or proclozine or procomp or stemetil or stemzine).mp.
- 126 profenamine/ or (profenamine or dibutil or ethopropazine or etopropazine or isothiazine or isothiazine or lysivane or parcidol or par-disol or parfezin\* or parkisol or parphezin or parsidol or parsitan or phenopropazine or “profenamine hydrochloride” or prophenamine or rochipel or rodipal or “rp 3356” or “sc 2538”).mp.
- 127 Promazine/ or (promazine or alofen or alophen or ampazine or amprazim or centractyl or delazin or esparin or lete or liranol or “neo hibernex” or neuroplegil or piarine or prazine or “pro tan” or promantine or promanyl or promilene or promwill or protactil or protactyl or romthiazine or romtiazin or “rp 3276” or sediston or sinophenin\* or sparine or tomil or varophen or verophen or “wy 1094”).mp.
- 128 propantheline bromide plus thiopropazate/ or ((propantheline adj4 thiopropazate) or “pro-banthine”).mp.
- 129 propiomazine/ or propiomazine maleate/ or (propiomazine or “cb 1678” or cb1678 or largon or propionylpromethazine or propiomazine or propromazine or dorevane or indorm or phenocetyl or propavan or “wy 1359”).mp.

- 130 propionylpromazine/ or (propionylpromazine or combelen or dipropiomazine or propiopromazine or tranvet).mp.
- 131 prothipendyl/ or (prothipendyl or “ay 5603” or ay5603 or azacon or “d 206” or d206 or dominal or inalforte or largophren or “lg 206” or lg206 or phrenotropin or prothipendil or protipendil or protipendyl or timovan or tolnate or tumovan).mp.
- 132 protoveratrine A plus protoveratrine B plus reserpine/ or protoveratrine A plus reserpine/ or pyrrobutamine plus reserpine/ or (protoveratrine or “veralba r” or verapene or “protalba-r” or pyrrobutamine or (sandril adj2 pyronil)).mp.
- 133 quinethazone plus reserpine/ (quinethazone or hydromax).mp.
- 134 Raclopride/ or raclopride tartrate/ or (raclopride or “flb-472” or “flb 472” or “fla-870” or “fla 870” or flb472 or fla870 or “a 40664” or a40664).mp.
- 135 Remoxipride/ or REMOXIPRIDE (nm) or (remoxipride or fla731 or “fla-731”).mp.
- 136 Reserpine/ or reserpine plus secbutabarbital/ or reserpine plus trichlormethiazide/ or (reserpine or abten or alkarau or alserin or anquil or apoplone\* or austrapine or boiserpine or crystoserpin or crystoserpine or elserpine or eroseprin or eskaserp or evraloid or hiserpia or hypersine or koglucoïd or lemiserp or maviserpine or “neo antitensol” or quiescin or “r-e-s” or “rau sed” or “rau-sed” or raudixoid or rauloydin or raunervil or raupina or raurine or roused or rousedan or rousedyl or rauserpine or rausingle or rautensin or rauwilid or rauwiloid or rauwolfaf or repoid or resercen or reserpamed or reserpen or reserpene or reserpex or reserpil or reserpin or reserpoid or resine or riserpa or rivasin or roxel or roxinoid or sandril or sedaraupin or serfin or serfolia or serolfia or serpalan or serpanray or serpasil or serpasol or serpate or serpen or serpena or serpentina or serpiloid or serpine or serpivite or sertabs or sertensin or sertina or “vio serpine” or “vio-serpine” or “v serp” or butiserpine or metatensin or naquival).mp.
- 137 rimcazole/ or (rimcazole or “bw 234” or “bw 234u” or bw234 or bw234u).mp.
- 138 Risperidone/ or (risperidone or belivon or consta or neripros or noprenia or “r 64766” or r64766 or “r-64766” or riperedon or risolept or rispen or risperdal or rispid or rispolet or rizodal or sequinan or zargus or zofredal).mp.
- 139 Ritanserine/ or RITANSERIN (nm) or (ritanserine or “r-55667” or r55667 or “r 55667”).mp.
- 140 romergoline/ or (romergoline or “fce 23884” or fce23884 or “ls 111871” or ls111871).mp.
- 141 savoxepine/ or (savoxepine or “cgp 19486” or “cgp 19486a” or cgp19486 or cgp19486a or cipazoxapine or savoxapine).mp.
- 142 (“sb 773812” or sb773812).mp.
- 143 seridopidine/ or (seridopidine or “acr 343” or acr343).mp.
- 144 setoperone/ or (setoperone or “r 52,245” or r 52245).mp.
- 145 Spiperone/ or Butyrophenones/ or Spiro Compounds/ or (spiperone or “r 5147” or r5147 or spiroperidol or spiroptan).mp.
- 146 sulforidazine/ or (sulforidazine or inofal or “tpn 12”).mp.
- 147 Sulpiride/ or (sulpiride or tepavil or lebopride or “vertigo meresa” or pontiride or sulperide or ekilid or sulp or sulpor or “vertigo-meresa” or dolmatil or digton oe aiglonyl or guastil or sulpitil or meresa or synedil or deponerton or arminol or neogama or eglonyl or sulpivert or “vertigo-neogama” or desisulpid or psicocen or dogmatil or “vertigo neogama”).mp.
- 148 tefludazine/ or (tefludazine or “lu 18 012” or “lu 18-012” or “lu 18012” or “lu18 012” or “lu18-012” or lu18012).mp. or tepirindole/ or (tepirindole or “hr 592” or hr592 or “ru 27592” or ru27592).mp.
- 149 thiopropazate/ or (thiopropazate or artalan or dartal or dartalan or dartin or “sc 7105” or thiopropazat).mp.
- 150 thioproperazine/ or thioproperazine methanesulfonate/ or (thiopropazine or “rp 7843” or thioperazine or majeptil or mayeptil or vontil).mp.
- 151 Thioridazine/ or (thioridazine or aldazine or apothioridazine or calmaril or mallorol or malloryl or meleril or mellaril or mellerets or mellerette\* or melleril or mellerzin or melleryl or melzine or mepiozin or orsanil or ridazin or ridazine or rideril or sonapax or thiomed or thioradazine or thioridacine or thioridazide or thioridazin or thioridazine or thioril or thiosia or thoridazine or thiozine or thioridazine-neurazpharm or tiordazin or tiordazine or “tp 21” or tpzl).mp.
- 152 Thiothixene/ or tiotixene/ or (tiotixene or cis thiothixene or “cp 12,252 1” or “cp 12252 1” or “cp 122521” or “cp12,252 1” or cp12252 1 or cp122521 or navan or navane or “nsc 108165” or nsc108165 or onaven or orbinamon or “p 4657 b” or “p 4657b” or p4657b or thiotixene or thiotixin or thiotixine or thixit).mp.
- 153 Tiapride Hydrochloride/ or Tiapride/ or (tiapride or delpral or “flo 1347” or “flo-1347” or flo1347 or itaprid or sereprile or thiapride or tiapridal or tiapridex or tiaprizal or equilibrium).mp.
- 154 timiperone/ or (timiperone or “dd 3480” or dd3480 or tolopelon).mp.
- 155 tranlycypromine plus trifluoperazine/ or ((tranlycypromine adj2 trifluoperazine) or jatrosom or parstelin or stelapar).mp.
- 156 triethylperazine/ or triethylperazin\*.mp.
- 157 Trifluoperazine/ or trifluoperazine derivative/ or (trifluoperazine or apotrifluoperazine or calmazine or eskazine or eskazinyl or espazine or fluoperazine or flupazine or fluperin or flurazin or “iremo-pierol” or jatroneural or leptazine or modalina or modiuor or nerolet or nylipton or operzine or oxyperazine or psyrazine or “sk and f 5019” or “skf 5019” or sporalon or stelazine or terfluzin\* or triflumed or trifluoperazide or trifluoperzine or trifluperazine or trifluoroperazine or trifluorperacine or trifluorperazine or trifluperazine or triflurin or triftazin or triftazine or triftazinum or trincalm or triozone or triptazine or triphthasine or triphthazine).mp.

158 Trifluoperidol/ or (trifluoperidol or "mcn jr 2498" or psicoperidol or "r 2498" or r2498 or trifluoperidol or triperidol or trisedyl or trisedil).mp.

159 Triflupromazine/ or (triflupromazine or adazine or fluopromazin or fluopromazine or fluorofen or "mc 4703" or mc4703 or nivoman or psyquil or siquil or "skf 4648 a" or "skf 4648a" or skf4648a or trifluopromazine or vespral or vesprin or vetame).mp.

160 umespirone/ or (umespirone or "kc 7218" or "kc 9172" or kc7218 or kc9172).mp.

161 vabicaserin/ or (vabicaserin or "sca 136" or sca136).mp.

162 zetidoline/ or (zetidoline or "dl 308" or "dl 308 it" or "dl 308it" or dl308 or dl308it).mp.

163 zicronapine/ or (zicronapine or "lu 31 130" or "lu 31-130" or "lu31 130" or "lu31-130").mp.

164 zoloperone/ or (zoloperone or "lr 511" or lr511).mp.

165 zuclopenthixol/ or zuclopenthixol acetate/ or zuclopenthixol decanoate/ or (zuclopenthixol or clopenthixol or cisordinol or sedanol or zuclopenthixol or clopixol).mp.

166 clonidine/ or (adesipress or arkamin or atensina or caprysin or catapres or catapresan or catasan or chlofazolin or chlophazolin or chlophelin or clinidine or clofelin or clofeline or clomidine or clondine or clonicef or clonidin or clonidine or clonipresan or clonistada or clonnirit or clophelin or clopheline or daipres or dcari or dichlorophenylaminoimidazoline or dixarit or duraclon or haemiton or hemiton or hypodine or isoglacon or jenloga or kapvay or "m 5041t" or melzin or normopresan or normopresin or paracefan or "st 155" or sulmidine or taitecin or "tenso timelet").mp.

167 Dexamethasone/ or (millicorten or maxidex or dexamethasone or dexpak or dexasone or oradexon or hexadecadrol or hexadrol or methylfluorprednisolone or decamet).mp.

168 lorazepam/ or (lorazepam or idalprem or sinestron or ativan or sedicepan or duralozam or orfidal or somagerol or apolorazepam or novolorazem or laubeel or donix or wy4036 or "wy 4036" or "wy-4036" or temesta or noloraz or tolid).mp.

169 midazolam/ or (midazolam or "ro 21-3981" or "ro 21 3981" or versed or "ro 213981" or dormicum).mp.

170 diazepam/ or (diazemuls or apaurin or seduxen or faustan or sibazon or valium or stesolid or relanium).mp.

171 donepezil/ or (donepezil or aricept or aricept or asenta or "e 2020" or "e2020" or eranz or memac or memorit).mp.

172 rivastigmine/ or (rivastigmine or "ena 713" or ena713 or exelon or nimvastid or prometax or rivastigmin or "sdz 212 713" or "sdz 212-713" or "sdz 212713" or "sdz ena 713" or "sdz ena713" or "sdz212 713" or "sdz212-713" or sdz212713).mp.

173 or/1-172 [\*\*\*\*AntiPsychotic, benzodiazepines, cholinergic antagoists drugs - added\*\*\*\*]

174 Confusion/ or Psychomotor Agitation/ or hallucinations/ or illusions/ or delusions/ or paranoid behavior/ or acute confusion/ or restlessness/ or (Psychomotor\* adj2 Agitat\*).mp. or hallucination/ or auditory hallucination/ or hallucinosis/ or visual hallucination/ or illusion/ or visual illusion/ or delusion/ or paranoia/ or paranoid psychosis/ or (inattention or inattentive\*).ti,ab.

175 ("icu syndrome" or (intensive adj2 care adj2 unit adj2 syndrome)).ti,ab.

176 delirium, dementia, amnesic, cognitive disorders/ or psychotic disorders/ or delirium/ postoperative delirium/ or (delirious\* or delirium).ti,ab. Or "disorders of higher cerebral function"/ or disorientation/ or organic brain syndrome/ or organic psychosyndrome/

177 (brain dysfunction/ and acute\*.ti,ab.) or ("acute brain dysfunction" or (acute adj2 brain adj2 dysfunction\*)) or "septic encephalopath").ti,ab.

178 (brain diseases/ and critical illness/) or brain disease/ and critically ill patient/

179 (brain diseases/ and sepsis/) or (brain disease/ and exp sepsis/ )

180 ("acute brain failure" or "acute organic psychosyndrome\*" or "acute brain syndrome" or "metabolic encephalopath\*" or "acute psycho-organic syndrome\*" or "clouded state" or "clouding of consciousness" or "exogenous psychosis" or "toxi psychosis" or "icu psychosis").ti,ab.

181 )brain diseases/ and (critical illness/ or Intensive Care/ or critical care/ or hospitalization/ or "length of stay"/ or patient admission/ or patient discharge/ or patient readmission/ or patient transfer/ or preoperative care/)) or (brain disease/ and ((intensive adj2 care).mp. or hospital care/ or exp intensive care/ or "length of stay"/ or hospital admission/ or hospital discharge/ or hospital readmission/ or hospital utilization/ or hospitalization/ or patient transport/ or preoperative period/ or preoperative care/ or preoperative evaluation/ or preoperative treatment/))

182 or/174-181 [\*\*\*\*Confusion, delirium terms\*\*\*\*]

183 173 and 182 [\*\*\*\*Base clinical set\*\*\*\*]

## Appendix 8. EBM Reviews - Health Technology Assessment Search Strategy

Database: EBM Reviews - Health Technology Assessment (2nd quarter 2017)

Search Strategy:

1 Antipsychotic drugs/ or Antipsychotic Agent/(antipsychotic\* or neuroleptic\* or (major adj2 (tranquilizer\* or tranquiliser\*))).mp.  
2 aceperone/ or (aceperone or acetabutone or acetobutone or "r 3248" or r3248).mp.  
3 Acepromazine/ or acepromazine maleate/ or (acepromazine or acetopromazine or vetranquil or acetylpromazine or acepromazine or calmivet or acetazine or notensil or plegicil or promace or soprintin or anatron or anergan or atravet or "cb 1522" or cb1522 or plegicin or plegicil or sedalin or soprintin).mp.  
4 aceprometazine/ or (aceprometazine or acepromethazine or acetylpromethazine).mp.  
5 acetophenazine / or (acetophenazine or acephenazine or "nsc 70600" or nsc70600 or "sch 6673" or sch6673 or tindal).mp.  
6 adopraine / or (adopraine or adopratin or "slv 313" or slv313).mp.  
7 alimemazine/ or (alimemazin or alimemasine or alimemazin\* or alimezine or "bayer 1219" or electrotrimeprazine or methylpromazine or palpex or "rp 6549" or rp6549 or trimeprazine or trimeprezine or varialgil or nedeltran or panectyl or repeltin or temaril or temaryl or teralen or teralene or theralen or theralene or valergan or vallergeran).mp.  
8 "alpha (4 fluorophenyl) 4 (5 fluoro 2 pyrimidinyl) 1 piperazinebutanol"/ or ("bms 181100" or bms181100 or "bmy 14802" or "bmy 14802 1" or "bmy 14802-1" or bmy14802 or "bmy14802 1" or "bmy14802-1" or bmy148021).mp.  
9 "alpha [1 [2 (1,4 benzodioxan 5 yloxy)ethyl] 3 pyrrolidinyl] 4 fluoroacetophenone"/ or ("s 16924" or s16924).mp.  
10 amitriptyline plus perphenazine/ or amitriptyline perphenazine/ or (amitriptyline or ((amitriptyline adj2 perphenazine) or "anxiress-d" or "duo-vil 2-10" or "duo-vil 2-25" or "duo-vil 4-10" or etrafon or etraphon or longopax or mutabon or mutanxion or mutaspline or "neuragon-a" or "neuragon-b" or pertriptyl or polybon or triavil or triptafen)).mp.  
11 aplindore/ or (aplindore or "dab 452" or dab452 or palindore or "way dab 452" or "way dab452").mp.)  
12 atypical antipsychotic agent/ or "1 cyclopropylmethyl 4 [2 (4 fluorophenyl) 2 oxoethyl]piperidine"/ or "1,2,3,4,8,9,10,10a octahydro 7bh cyclopenta[b][1,4]diazepino[6,7,1 hi]indole"/ or "2 amino n [4 [4 (1,2 benzisothiazol 3 yl) 1 piperazinyl]butyl]benzamide"/ or "2 chloro 11 (3 dimethylaminopropylidene)morphanthridine"/ or "4 (4 fluorophenyl) 1,2,3,6 tetrahydro 1 [4 (1,2,4 triazol 1 yl)butyl]pyridine"/ or "4,9 dibromo 6 (4 methyl 1 piperazinyl)benzo[b]pyrrolo[3,2,1 jk][1,4]benzodiazepine"/ or "7 [3 [4 (2,3 dimethylphenyl) 1 piperazinyl]propoxy] 2(1h) quinolinone"/ or "7 chloro 2 [[1 (2 methoxyphenyl) 4 piperidyl]methylaminomethyl] 1,4 benzodioxan"/ or "8 fluoro 4 [3 (2 methoxyethyl) 4 methyl 1 piperazinyl] 2 methyl 10h thieno[2,3 b][1,5]benzodiazepine"/ or atypical antipsychotic agent/ or (atypical adj2 (antipsychotic\* or neuroleptic\*)).mp. or abaperidone/ or (abaperidone or "fi 8602" or fi8602).mp. or alentamol/ or (alentamol or alentemol or "u 66444b" or "u 68552b" or "u 68553b" or u66444b or u68552b or u68553b).mp. or amisulpride/ or (aminosultopride or amisulpride or amisulpridum or "dan 2163" or dan2163 or sertol or socian or solian).mp. or amperozide/ or (amperozide or "fg 5606" or fg5606).mp. or aripiprazole/ or (aripiprazole or abilify or abilitat or "opc 14597" or opc14597).mp. or asenapine/ or (asenapine or "org 5222" or org5222 or saphris or sycrest).mp. or batelapine/ or (batelapine or "cgs 13429" or cgs13429).mp. or belaperidone/ or (belaperidone or balaperidone or "lu 111995" or lu111995).mp. or bifeprunox/ or (bifeprunox or "du 127090" or du127090).mp. or elopiprazole/ or emonapride/ or (emonapride or emirace or nemonapride or "ym 09151" or "ym 09151 02" or "ym 09151 2" or "ym 09151-02" or "ym 09151-2" or ym09151 or "ym09151 02" or "ym09151 2" or "ym09151-02" or "ym09151-2" or ym0915102 or ym091512).mp. or flumetazapine/ or (flumetazapine or "ly 120363" or ly120363).mp. or fluoxetine plus olanzapine/ or ((fluoxetine adj2 olanzapine) or symbyax).mp. or fluperlapine/ or (fluperlapine or "nb 106689" or nb106689).mp. or iloperidone/ or (iloperidone or fanapt or fanaptum or "hp 873" or hp873 or "ilo 522" or ilo522 or zomaril).mp. or lurasidone/ or (lurasidone or latuda or "mk 3756" or mk3756 or "sm 13496" or sm13496 or "smp 13496" or smp13496).mp. or melperone/ or (melperone or bunil or buronil or eunerpan or "fg 5111" or fg5111 or flubuperone or melperon or methylperone or metylperone or metylperonum).mp. or "n (2 chloro 6 methylergolin 8alpha yl)pivalamide"/ or ("sdz 208 912" or "sdz 208-912" or "sdz 208912" or "sdz 912" or "sdz hdc 912" or "sdz hdc912" or "sdz208 912" or "sdz208-912" or sdz208912 or sdz912).mp. or "n (2,6 dimethylergolin 8alpha yl)pivalamide"/ or ("sdz 208 911" or "sdz 208-911" or "sdz 208911" or "sdz 911" or "sdz hac 911" or "sdz hac911" or "sdz208 911" or "sdz208-911" or sdz208911 or sdz911).mp. or "n cyclohexyl 4 [4 (4 fluorophenyl) 4 oxobutyl] 1 piperazinecarboxamide"/ or ("fg 5803" or fg5803).mp. or norclozapine/ or (norclozapine or demethylclozapine or desmethylclozapine).mp. or ocaperidone/ or (ocaperidone or "r 79598" or r79598).mp. or olanzapine/ or (olanzapine or anzatic or "dopin tab" or "jolyon md" or lanopin or lanzac or "ly 170053" or ly170053 or miltolan or midax or olace or oladay or olan or olandus or olanex or olansek or olapin or olazax or oleanz or olexar or oltal or olzap or onza or "ozapin md" or psychozap or relprev or zalasta or zelta or zydis or zypadhera or zyprex or zyprexa or zyprexav).mp. or paliperidone/ or (paliperidone or invega or "paliperidone palmitate" or "r 76477" or r76477 or "ro 76477" or "ro 92670" or ro76477 or ro92670 or xeplion).mp. or panemesine/ or (panemesine or "emd 57445" or emd57445).mp. or pentiapipe/ or pentiapipe maleate/ or (pentapipe or "cgs 10746" or cgs10746 or "cgs 10746b" or cgs10746b).mp. or perlapine/ or (perlapine or "aw 14'2333" or "aw 142333" or aw142333 or perlapin).mp. or perospirone/ or



(perospirone or lullan or "sm 9018" or sm9018).mp. or pridopidine/ or (pridopidine or "acr 16" or acr16 or "asp 2314" or asp2314 or "fr 310826" or fr310826 or huntexil).mp. or quetiapine/ or (quetiapine or "ici 204636" or "ici 204646" or ici204636 or ici204646 or seroquel or socalm or tienapine).mp. or remoxipride/ or (remoxipride or "a 33547" or a33547 or "fla 731" or fla731 or roxiam).mp. or rilapine/ or rilapine.mp. or sertindole/ or (sertindole or "lu 23174" or lu23174 or "s 1991" or s1991 or serdolect or serlect).mp. or sulpiride/ or (sulpiride or abilit or aiglonyl or arminol or dobren or dogmatil or dogmatyl or dolmatil or eglonyl or equilid or "fk 880 " or fk880 or isnamide or levobren or levopraid or levosulpiride or meresa or miradol or neogama or sulfiride or sulpivot or sulpyride or synedil or vipral).mp. or sultopride/ or (sultopride or barnetil or barnotil or "ms 5024" or ms5024 or sulfopride).mp. or tenilapine/ or tenilapine.mp. or tiospirone/ or (tiospirone or "bmy 13859" or bmy13859 or "mj 13859" or "mj 13859 1" or "mj 13859-1" or mj13859 or "mj13859 1" or "mj13859-1" or mj138591 or tiaspirone).mp. or volinanserine/ or (volinanserine or "m 100907" or m100907 or "mdl 100151" or "mdl 100907" or mdl100151 or mdl100907).mp. or ziprasidone/ or (ziprasidone or "cp 88059" or "cp 88059 01" or "cp 88059 27" or "cp 88059-01" or "cp 88059-27" or "cp 8805901" or "cp 8805927" or cp88059 or "cp88059 01" or "cp88059 27" or "cp88059-01" or "cp88059-27" or cp8805901 or cp8805927 or geodon or zeldox or zeldrox or zipsydon).mp. or zotepine/ or (zotepine or lodopin or nipolept).mp.

13 Azaperone/ or (azaperone or "r-1929" or r1929 or sedaperone or stresnil).mp.)

14 Benperidol/ or (benperidol or anquil or benperidone or benzoperidol or benzperidol or benperidolneuraxpharm or "cb 8089" or cb8089 or frenactyl or frenactil or glianimon or "mcn jr 4584" or "mcn jr4584" or phenactil or "r 4584" or r4584).mp.

15 berupipam/ or (berupipam or "nnc 22 0010" or "nnc22 0010").mp.

16 bitopertin/ or (bitopertin or paliflutine or "r 1678" or r1678 or "rg 1678" or rg1678 or "ro 4917838" or ro4917838).mp.

17 blonanserine/ or (blonanserine or "ad 5423" or ad5423 or lonasen).mp.

18 brexpiprazole or (brexpiprazole or "opc 34712" or opc34712).mp.

19 brofexine/ or (brofexine or dimetabrone or "fi 6820" or fi6820).mp.

20 bromospiperone/ or (bromospiperone or bromospiroperidol).mp. (0)

21 bromperidol/ or bromperidol decanoate/ or (bromperidol or impromen or "r 11,333" or "r 11333" or "r11,333" or r11333 or tesoprel or "impromen decanoate" or "r 46,541" or "r 46541" or "r46,541" or r46541).mp.

22 Butaclamol/ or Dibenzocycloheptenes/ or ("ay 23,028" or "ay 23028" or "ay23,028" or "ay-23028" or ay23028 or butaclamol).mp.

23 butaperazine/ or (butaperazine or "ahr 3000" or "bayer 1362" or butaperazinum or butyrylperazin or butyrylperazine or megalectil or randolectil or randolectyl or repoise or "riker 595" or tyrylen).mp.

24 carfenazine/ or (carfenazine or carfenazinum or carphenazine or "nsc 71755" or nsc71755 or procethazine or proketazine or "wy 2445" or wy2445).mp.

25 cariprazine/ or (cariprazine or "mp 214" or mp214 or "rgh 188" or rgh188).mp.

26 carpipramine/ or (carpipramine or carbadipimidine or defecton or defekton or prazinil or "pz 1511" or pz1511 or "rp 21679" or rp21679).mp.

27 carvotroline/ or (carvotroline or "wy 47791" or wy47791).mp.

28 centbutindole/ or centbutindole.mp.

29 chlorothiazide plus reserpine/ or (chlorothiazide or "diupres-250" or "diupres-500").mp.

30 chlorphenethazine/ or (chlorphenethazine or chlorfenethazine or elroquil or marophen).mp.

31 chlorproethazine/ or (chlorproethazine or neuriplege or "rp 4909" or rp4909).mp.

32 chlorpromazine/ or chlorpromazine plus dexamphetamine/ or chlorpromazine sulfoxide/ or (chlorpromazine or "2601 a" or "4560 r p" or aminasin or aminasine or aminazin or aminazine or ampliactil or amplitil or ancholactil or aspersinal or bellacina or cepezet or chlomazine or "chlor pz" or chloractil or chlorazine or chlorbromasin or chlorderazine or chlorderazin or chlormazine or chlorpromanyl or chlorpromazin or chlorpromed or clonazine or clordelazin or clorpromaz or clorpromazine or clozine or contomin or duncan or elmarin or esmino or fenactil or hibanil or hibernal or hibernal or "hl 3746" or "hl 5746" or klorproman or klorpromazin or klorpromex or laractyl or largactil or largactyl or matcine or megaphen or megatil or "ml 5746" or neomazine or neurazine or novomazina or phenathyl or plegomazin or plegomazine or proma or promacid or promactil or promapar or promazil or promexin or propaphen or propaphenin or prozil or prozin or psychozine or psynor or "rp 4560" or sanopron or "skf 2601 a" or solidon or sonazine or taroctil or taroctyl or "thor prom" or thorazene or thorazine or torazina or "vegetamin a" or "vegetamin b" or winsumin or wintamine or wintermin or zuledin or "thora-dex" or opromazine or secotil).mp.

33 Chlorprothixene/ or (chlorprothixene or chloprothixene or "chlor prothixene" or chlorprothixene or chlorprothixen or chlorprothixenechloride or chlorprotixen or chlorprotixene or chlothixen or "n 714" or "n 7714" or "ro 4 0403" or "ro 40403" or taractan or tarasan or traquilan or troxen or truxal or truxaleta or truxaletten).mp.

34 cinuperone/ (cinuperone or "hr 375" or hr375).mp.

35 clocapramine/ or (clocapramine or "y 4153" or y4153).mp.

36 cloflumide mesilate/ or ("cloflumide mesylate" or "vufb 15496" or vufb15496).mp.

- Antipsychotics for treatment of delirium in hospitalised non-ICU patients (Review) 103  
Copyright © 2018 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

69 Haloperidol/ or haloperidol decanoate/ or (haloperidol or alased or aloperidin\* or avant or binison or brotopon or celenase or cereen or cerenace or cizoren or depidol or dores or dozic or duraperidol or "einalon s" or fortunat or govotil or haldol or halidol or "halo-p" or halojust or halomed or haloneural or haloper or haloperil or haloperin or haloperitol or halopidol or halopol or halosten or haricon or "haridol-d" or keselan or linton or "lodomer-2" or "mcn jr 1625" or "mcn jr1625" or mixidol or novoperidol or "nsc 170973" or nsc170973 or peluces or perida or peridol or peridor or "r 1625" or r1625 or selezyme or seranace or serenace or serenase or serenelfi or siegoperidol or sigaperidol or trancodol or pericate or "r 13,672" or "r 13672" or senorm).mp.

70 hexamethonium chloride plus reserpine/ or (hexamethonium or reserthonium).mp.

71 hydralazine plus reserpine/ or hydrochlorothiazide plus potassium chloride plus reserpine/ or hydrochlorothiazide plus reserpine/ or (dralserp or (hydralazine adj2 reserpine) or "serpasil-apresoline" or "hydropresor dichlotride s" or "h.r.-50" or "hydro-reserp" or hydrochlorothiazide or hydroserpine or "medeserpine co" or "serpasil-esidrix").mp.

72 hydrochlorothiazide plus reserpine plus secbutabarbita/ or ((hydrochlorothiazide adj2 reserpine adj2 secbutabarbita) or butiserpazide).mp.

73 hydroflumethiazide plus potassium chloride plus reserpine/ or ((hydroflumethiazide adj4 reserpine) or rautrax).mp.

74 hydroflumethiazide plus reserpine/ or ((hydroflumethiazide adj2 reserpine) or salutensin\*).mp.

75 isofloxythepin/ or (isofloxythepin or "vufb 10662").mp.

76 isomolpan/ or (isomolpan or "cgs 15855" or "cgs 15855 a" or "cgs 15855a" or cgs15855 or cgs15855a).mp.

77 isopropamide iodide plus prochlorperazine maleate/ or ((isopropamide adj4 prochlorperazine) or "combid spansule").mp.

78 lenperone/ or (lenperone or "ahr 2277" or ahr2277 or elanone).mp.

79 levomepromazine/ or (levomepromazine or "apo-methoprazine" or "bayer 1213" or "cl 36467" or "cl 39743" or cl36467 or cl39743 or hiranamin or mepromazine or levium or promazine or levomeprazine or levopromazin\* or levoprome or levozin or mepromazine or methotrimprazine or methozane or milezin or minozinan or neozine or neuractil or neurocil or nirvan or nozinan or "rp 7044" or rp7044 or sinogan or "sk and f 5116" or "skf 5116" or skf5116 or tiscerin or tiscerin or veractil).mp.

80 lithium/ or lithium.mp.

81 Loxapine/ or loxapine succinate/ or (loxapine or adasuve or "alxz 004" or alxz004 or "az 004" or az004 or "cl 62,362" or "cl 62362" or "cl62,362" or cl62362 or "cl 71563" or "cl-71563" or cl71563 or loxapinsuccinate or cloxazepin\* or loxapane or loxapin\* or loxitane or oxilapine or "sum 3170" or sum3170 or daxolin or desconex or loxapac).mp.

82 maroxepine/ or maroxepine.mp.

83 mazapertine/ or (mazapertine or "rwj 37796" or rwj37796).mp.

84 mepiprazole/ or meprobamate plus promazine/ or (mepiprazole or "emd 16923" or emd16923 or psigodal or prozine or meproba-mate).mp.

85 Mesoridazine/ or Phenothiazines/ or Tranquilizing Agents/ or mesoridazine besylate/ or (mesoridazin\* or esoridazine or lidanar or lidanil or mesorin or "nc 123" or (thioridazine adj2 sulfoxide) or "tps 23" or serentil).mp.

86 methamphetamine plus reserpine/ or ((methamphetamine adj2 reserpine) or "du-oria").mp.

87 Methiothepin/ or Dibenzothiepins/ or Piperazines/ or methyclothiazide plus reserpine/ or (methiothepin\* or metitepine).mp.

88 methopromazine/ or (methopromazine or methoxypropromazine or metopromazine or "diutensen-r").mp.

89 Methotrimprazine/ or (levopromazine or tizercine or methotrimprazine or levomepromazine or levomeprazin or tiscerin or tizertsin).mp.

90 metofenazate/ or (metofenazate or frenolon or metaphenazine or methophenazine or metophenazine or phrenolon).mp.

91 Molindone/ or indoles/ or (molindon\* or "en 1733a" or en1733a or lidone or moban or molindor).mp.

92 moperone/ or (moperone or luvatren or luvatrena or "methyl peridol" or methylperidol\* or moperon or "r 1658").mp.

93 "n [(1 butyl 2 pyrrolidinyl)methyl] 2,3 dihydro 2 methyl 5 sulfamoyl 7 benzofurancarboxamide"/ or ("y 20024" or y20024).mp.

94 "n [3 (4 fluorophenyl) 3 (4 phenylphenoxy)propyl]sarcosine"/ or ("alx 5407" or alx5407 or NFPS).mp.

95 "n [4 [2 (6 cyano 1,2,3,4 tetrahydro 2 isoquinolinyl)ethyl]cyclohexyl] 4 quinolinecarboxamide"/ or ("sb 277011" or "sb 277011a" or sb277011 or sb277011a).mp.

96 neboglamine/ or (neboglamine or "cr 2249" or cr2249 or "xy 2401" or xy2401).mp.

97 nicotinic acid plus pentetrazole plus reserpine/ or ((nicotinic adj4 pentetrazole adj4 reserpine) or (nicozol adj2 reserpine)).mp.

98 noctran/ or noctran.mp.

99 norchlorpromazine/ or (norchlorpromazine or demethylchlorpromazine or demonomethylchlorpromazine or desmethylchlorpromazine or desmonomethylchlorpromazine or monodesmethylchlorpromazine).mp.

100 Ondansetron/ or Imidazoles/ or (ondansetron or gr38032f or "gr 38032f" or "sn 307" or sn307 or "gr-38032f" or "sn-307" or zofran).mp.

101 oxiperomide/ or (oxiperomide or "r 4714" or r4714).mp.

- 102 oxypertine/ or (oxypertin\* or “cl 77328” or cl77328 or equipertine or forit or opertil or oxipertin or oxypertin or “win 18501 2” or “win 18501-2” or “win 185012” or “win18501 2” or “win18501-2” or win185012).mp.
- 103 oxyprothepine/ or oxyprothepine decanoate/ or (oxyprothepine or oxyprothepin).mp.
- 104 pecazine/ or (pecazine or lacumin or mepasin or mepazine or nothiazine or “p 391” or pacatal or pacatol or pactal or papital or paxital or pecazine or “w 1224”).mp.
- 105 Penfluridol/ or (penfluridol or “mcn jr 16,341” or “mcn jr 16341” or micefal or “r 16,341” or “r 16341” or semap or “r 16341” or “r-16341” or r16341).mp.
- 106 Perazine/ or (perazine or taxilan).mp.
- 107 pentaerythrityl tetranitrate plus reserpine/ or pentaerythrityl tetranitrate plus reserpine plus secbutabarbital/ or (pentaerythrityl or pentaserpine or respet or pentraline).mp.
- 108 pentobarbital plus reserpine/ or (“nambu-serpine” or (pentobarbital adj2 reserpine)).mp.
- 109 perazine/ or (perazine or “p 725” or pernazine or taxilan).mp.
- 110 periciazine/ or (periciazine or aolept or neulactil or neuleptil\* or periciazinum or pericyazine or properciazine or propericiazin or propericiazine or “rp 8909” or “skf 20716”).mp.
- 111 perimetazine/ or (perimetazine or “1317 an” or “an 1317” or an1317 or leptyl or perimethazine).mp.
- 112 Perphenazine/ or perphenazine decanoate/ or perphenazine enanthate.mp. or (perphenazine or chlorperphenazine or chlorpiprazine or chlorpiprozine or decentan or etaperazine or ethaperazine or “f-mon” or fentazin or leptopsique or peratsin or perfenazine or perferazine or pernamed or perphenan or perphenazin\* or “perzine-p” or porazine or “sch 3940” or thilatazin or tranquisan or trifalon or trilafan or trilafon or trilifan or triliphan or triomin).mp.
- 113 (“pf 217830” or pf217830 or “pf 2400013” or pf2400013 or “pf 3463275” or pf3463275).mp.
- 114 phenobarbital plus reserpine/ or phenobarbital plus reserpine plus theobromine/ or phenobarbital plus reserpine plus thiamine.mp. or ((phenobarbital adj2 reserpine) or “solfo-serpine” or bromoserpin or “theo-serp” or “theobarb-r” or theoserpin or besertal or “neo-slowten”).mp.
- 115 picobenzide/ or (picobenzide or dosetil or “m 14012 4” or “ma 14012” or picobenzamide).mp.
- 116 piflutixol/ or piflutixol.mp.
- 117 pimavanserine/ or (pimavanserine or “acp 103” or acp103).mp.
- 118 pimethixene/ or (pimethixene or “bp 400” or “bp 400 e” or “bp 400e” or bp400 or bp400e or muricalm or pimetixin).mp.
- 119 Pimozide/ or (pimozide or antalon or “mcn jr 6238” or opiran or orap or pimocide or pimoride or pinozide or pizide or “r 6238” or r6238).mp.
- 120 pipamperone/ or (pipamperone or dipeperon or dipiperon or “dl piperonyl” or floropipamide or “piperonyl of pripamperone of r 3345” or r3345).mp.
- 121 piperacetazine/ or (piperacetazine or “pc 1421or pc1421” or quide).mp.
- 122 pipotiazine/ or pipotiazine palmitate/ or pipotiazine undecenoate/ or (pipotiazine or “9366 rp” or piportil or pipothiazine or “rp 19366” or rp19366 or “il 19552” or il19552 or “rp 19552” or rp19552 or rp 19551).mp.
- 123 pirenperone/ or polythiazide plus reserpine/ or (pirenperone or “r 47,465” or “r 47465” or “r 50656” or “r47,465” or r47465 or r50656 or “renese r” or “renese-r”).mp.
- 124 pomaglumetad methionil/ or (“pomaglumetad methionil” or “ly 2140023” or ly2140023).mp.
- 125 Prochlorperazine/ or prochlorperazine edisylate/ or prochlorperazine maleate/ or (compazine or prochlorperazine or “6140 rp” or antinaus or “bayer a 173” or “bayer 173” or capazine or chlormepazine or chlorpeazine or chlorperazine or compro or dicopal or emelent or klometil or kronocin or meterazine or metherazine or nautisol or nipodal or normalmin or pasotomin or prochlor or prochlorpemazine or prochlorperacine or prochlorperzine or prochlorpromazine or prochlorperazine or procot or “rp 6140 ir rp6140” or “sk and f 4657” or “skf 4657” or skf4657 or tementil or temetil or buccastem or dhaperazine or emeteral or emetiral or nibromin or proclozine or procomp or stemetil or stemzine).mp.
- 126 profenamine/ or (profenamine or dibutil or ethopropazine or etopropazine or isothiazine or isothiazine or lysivane or parcidol or par-disol or parfezin\* or parkisol or parphezin or parsidol or parsitan or phenopropazine or “profenamine hydrochloride” or prophenamine or rochipel or rodipal or “rp 3356” or “sc 2538”).mp.
- 127 Promazine/ or (promazine or alofen or alophen or ampazine or amprazim or centractyl or delazin or esparin or lete or liranol or “neo hibernex” or neuroplegil or piarine or prazine or “pro tan” or promantine or promanyl or promilene or promwill or protactil or protactyl or romthiazine or romtiazin or “rp 3276” or sediston or sinophenin\* or sparine or tomil or varophen or verophen or “wy 1094”).mp.
- 128 propantheline bromide plus thiopropazate/ or ((propantheline adj4 thiopropazate) or “pro-banthine”).mp.
- 129 propiomazine/ or propiomazine maleate/ or (propiomazine or “cb 1678” or cb1678 or largon or propionylpromethazine or propiomazine or propromazine or dorevane or indorm or phenocetyl or propavan or “wy 1359”).mp.

- 130 propionylpromazine/ or (propionylpromazine or combelen or dipropiomazine or propiopromazine or tranvet).mp.
- 131 prothipendyl/ or (prothipendyl or “ay 5603” or ay5603 or azacon or “d 206” or d206 or dominal or inalforte or largophren or “lg 206” or lg206 or phrenotropin or prothipendil or protipendil or protipendyl or timovan or tolnate or tumovan).mp.
- 132 protoveratrine A plus protoveratrine B plus reserpine/ or protoveratrine A plus reserpine/ or pyrrobutamine plus reserpine/ or (protoveratrine or “veralba r” or verapene or “protalba-r” or pyrrobutamine or (sandril adj2 pyronil)).mp.
- 133 quinethazone plus reserpine/ (quinethazone or hydromax).mp.
- 134 Raclopride/ or raclopride tartrate/ or (raclopride or “flb-472” or “flb 472” or “fla-870” or “fla 870” or flb472 or fla870 or “a 40664” or a40664).mp.
- 135 Remoxipride/ or REMOXIPRIDE (nm) or (remoxipride or fla731 or “fla-731”).mp.
- 136 Reserpine/ or reserpine plus secbutabarbital/ or reserpine plus trichlormethiazide/ or (reserpine or abten or alkarau or alserin or anquil or apoplone\* or austrapine or boiserpine or crystoserpin or crystoserpine or elserpine or eroseprin or eskaserp or evraloid or hiserpia or hypersine or koglucoïd or lemiserp or maviserpine or “neo antitensol” or quiescin or “r-e-s” or “rau sed” or “rau-sed” or raudixoid or rauloydin or raunervil or raupina or raurine or raurine or roused or rousedan or rousedyl or rouserpine or rausingle or rautensin or rauwilid or rauwiloid or rauwolfaf or repoid or resercen or reserpamed or reserpen or reserpene or reserpex or reserpil or reserpin or reserpoid or resine or riserpa or rivasin or roxel or roxinoid or sandril or sedaraupin or serfin or serfolia or serolfia or serpalan or serpanray or serpasil or serpasol or serpate or serpen or serpena or serpentina or serpiloid or serpine or serpivite or sertabs or sertensin or sertina or “vio serpine” or “vio-serpine” or “v serp” or butiserpine or metatensin or naquival).mp.
- 137 rimcazole/ or (rimcazole or “bw 234” or “bw 234u” or bw234 or bw234u).mp.
- 138 Risperidone/ or (risperidone or belivon or consta or neripros or noprenia or “r 64766” or r64766 or “r-64766” or riperon or risolept or rispen or risperdal or rispid or rispolet or rizodal or sequinan or zargus or zofredal).mp.
- 139 Ritanserine/ or RITANSERIN (nm) or (ritanserine or “r-55667” or r55667 or “r 55667”).mp.
- 140 romergoline/ or (romergoline or “fce 23884” or fce23884 or “ls 111871” or ls111871).mp.
- 141 savoxepine/ or (savoxepine or “cgp 19486” or “cgp 19486a” or cgp19486 or cgp19486a or cipazoxapine or savoxapine).mp.
- 142 (“sb 773812” or sb773812).mp.
- 143 seridopidine/ or (seridopidine or “acr 343” or acr343).mp.
- 144 setoperone/ or (setoperone or “r 52,245” or r 52245).mp.
- 145 Spiperone/ or Butyrophenones/ or Spiro Compounds/ or (spiperone or “r 5147” or r5147 or spiroperidol or spiroptan).mp.
- 146 sulfuridazine/ or (sulfuridazine or inofal or “tpn 12”).mp.
- 147 Sulpiride/ or (sulpiride or tepavil or lebopride or “vertigo meresa” or pontiride or sulperide or ekilid or sulp or sulpor or “vertigo-meresa” or dolmatil or digton oe aiglonyl or guastil or sulpitil or meresa or synedil or deponerton or arminol or neogama or eglonyl or sulpivert or “vertigo-neogama” or desisulpid or psicocen or dogmatil or “vertigo neogama”).mp.
- 148 tefludazine/ or (tefludazine or “lu 18 012” or “lu 18-012” or “lu 18012” or “lu18 012” or “lu18-012” or lu18012).mp. or tepirindole/ or (tepirindole or “hr 592” or hr592 or “ru 27592” or ru27592).mp.
- 149 thiopropazate/ or (thiopropazate or artalan or dartal or dartalan or dardan or “sc 7105” or thiopropazat).mp.
- 150 thioproperazine/ or thioproperazine methanesulfonate/ or (thiopropazine or “rp 7843” or thioperazine or majeptil or mayeptil or vontil).mp.
- 151 Thioridazine/ or (thioridazine or aldazine or apothioridazine or calmaril or mallorol or malloryl or meleril or mellaril or mellerets or mellerette\* or melleril or mellerzin or melleryl or melzine or mepiozin or orsanil or ridazin or ridazine or rideril or sonapax or thiomed or thioradazine or thioridacine or thioridazide or thioridazin or thioridazine or thioril or thiosia or thioridazine or thiozine or thioridazineneurazpharm or tiordazin or tiordazine or “tp 21” or tpzl).mp.
- 152 Thiothixene/ or tiotixene/ or (tiotixene or cis thiothixene or “cp 12,252 1” or “cp 12252 1” or “cp 122521” or “cp12,252 1” or cp12252 1 or cp122521 or navan or navane or “nsc 108165” or nsc108165 or onaven or orbinamon or “p 4657 b” or “p 4657b” or p4657b or thiotixene or thiotixin or thiotixine or thixit).mp.
- 153 Tiapride Hydrochloride/ or Tiapride/ or (tiapride or delpral or “flo 1347” or “flo-1347” or flo1347 or itaprid or sereprile or thiapride or tiapridal or tiapridex or tiaprizal or equilibrium).mp.
- 154 timiperone/ or (timiperone or “dd 3480” or dd3480 or tolopelon).mp.
- 155 tranlycypromine plus trifluoperazine/ or ((tranlycypromine adj2 trifluoperazine) or jatrosom or parstelin or stelapar).mp.
- 156 triethylperazine/ or triethylperazin\*.mp.
- 157 Trifluoperazine/ or trifluoperazine derivative/ or (trifluoperazine or apotrifluoperazine or calmazine or eskazine or eskazinyl or espazine or fluoperazine or flupazine or fluperin or flurazin or “iremo-pierol” or jatroneural or leptazine or modalina or modiuor or nerolet or nylipton or operzine or oxyperazine or psyrazine or “sk and f 5019” or “skf 5019” or sporalon or stelazine or terfluzin\* or triflumed or trifluoperazide or trifluoperzine or trifluperazine or trifluoroperazine or trifluorperacine or trifluorperazine or trifluperazine or triflurin or triftazin or triftazine or triftazinum or trincalm or triozone or triptazine or triphthasine or triphthazine).mp.

158 Trifluoperidol/ or (trifluoperidol or "mcn jr 2498" or psicoperidol or "r 2498" or r2498 or trifluoperidol or triperidol or trisedyl or trisedil).mp.

159 Triflupromazine/ or (triflupromazine or adazine or fluopromazin or fluopromazine or fluorofen or "mc 4703" or mc4703 or nivoman or psyquil or siquil or "skf 4648 a" or "skf 4648a" or skf4648a or trifluopromazine or vespral or vesprin or vetame).mp.

160 umespirone/ or (umespirone or "kc 7218" or "kc 9172" or kc7218 or kc9172).mp.

161 vabicaserin/ or (vabicaserin or "sca 136" or sca136).mp.

162 zetidoline/ or (zetidoline or "dl 308" or "dl 308 it" or "dl 308it" or dl308 or dl308it).mp.

163 zicronapine/ or (zicronapine or "lu 31 130" or "lu 31-130" or "lu31 130" or "lu31-130").mp.

164 zoloperone/ or (zoloperone or "lr 511" or lr511).mp.

165 zuclopenthixol/ or zuclopenthixol acetate/ or zuclopenthixol decanoate/ or (zuclopenthixol or clopenthixol or cisordinol or sedanol or zuclopenthixol or clopixol).mp.

166 clonidine/ or (adesipress or arkamin or atensina or caprysin or catapres or catapresan or catasan or chlofazolin or chlophazolin or chlophelin or clinidine or clofelin or clofeline or clomidine or clondine or clonicef or clonidin or clonidine or clonipresan or clonistada or clonnirit or clophelin or clopheline or daipres or dcari or dichlorophenylaminoimidazoline or dixarit or duraclon or haemiton or hemiton or hypodine or isoglacon or jenloga or kapvay or "m 5041t" or melzin or normopresan or normopresin or paracefan or "st 155" or sulmidine or taitecin or "tenso timelet").mp.

167 Dexamethasone/ or (millicorten or maxidex or dexamethasone or dexpak or dexasone or oradexon or hexadecadrol or hexadrol or methylfluorprednisolone or decamet).mp.

168 lorazepam/ or (lorazepam or idalprem or sinestron or ativan or sedicepan or duralozam or orfidal or somagerol or apolorazepam or novolorazem or laubeel or donix or wy4036 or "wy 4036" or "wy-4036" or temesta or noloraz or tolid).mp.

169 midazolam/ or (midazolam or "ro 21-3981" or "ro 21 3981" or versed or "ro 213981" or dormicum).mp.

170 diazepam/ or (diazemuls or apaurin or seduxen or faustan or sibazon or valium or stesolid or relanium).mp.

171 donepezil/ or (donepezil or aricept or aricept or asenta or "e 2020" or "e2020" or eranz or memac or memorit).mp.

172 rivastigmine/ or (rivastigmine or "ena 713" or ena713 or exelon or nimvastid or prometax or rivastigmin or "sdz 212 713" or "sdz 212-713" or "sdz 212713" or "sdz ena 713" or "sdz ena713" or "sdz212 713" or "sdz212-713" or sdz212713).mp.

173 or/1-172 [\*\*\*\*AntiPsychotic, benzodiazepines, cholinergic antagoists drugs - added\*\*\*\*]

174 Confusion/ or Psychomotor Agitation/ or hallucinations/ or illusions/ or delusions/ or paranoid behavior/ or acute confusion/ or restlessness/ or (Psychomotor\* adj2 Agitat\*).mp. or hallucination/ or auditory hallucination/ or hallucinosis/ or visual hallucination/ or illusion/ or visual illusion/ or delusion/ or paranoia/ or paranoid psychosis/ or (inattention or inattentive\*).ti,ab.

175 ("icu syndrome" or (intensive adj2 care adj2 unit adj2 syndrome)).ti,ab.

176 delirium, dementia, amnesic, cognitive disorders/ or psychotic disorders/ or delirium/ postoperative delirium/ or (delirious\* or delirium).ti,ab. Or "disorders of higher cerebral function"/ or disorientation/ or organic brain syndrome/ or organic psychosyndrome/

177 (brain dysfunction/ and acute\*.ti,ab.) or ("acute brain dysfunction" or (acute adj2 brain adj2 dysfunction\*)) or "septic encephalopath").ti,ab.

178 (brain diseases/ and critical illness/) or brain disease/ and critically ill patient/

179 (brain diseases/ and sepsis/) or (brain disease/ and exp sepsis/ )

180 ("acute brain failure" or "acute organic psychosyndrome\*" or "acute brain syndrome" or "metabolic encephalopath\*" or "acute psycho-organic syndrome\*" or "clouded state" or "clouding of consciousness" or "exogenous psychosis" or "toxi psychosis" or "icu psychosis").ti,ab.

181 )brain diseases/ and (critical illness/ or Intensive Care/ or critical care/ or hospitalization/ or "length of stay"/ or patient admission/ or patient discharge/ or patient readmission/ or patient transfer/ or preoperative care/)) or (brain disease/ and ((intensive adj2 care).mp. or hospital care/ or exp intensive care/ or "length of stay"/ or hospital admission/ or hospital discharge/ or hospital readmission/ or hospital utilization/ or hospitalization/ or patient transport/ or preoperative period/ or preoperative care/ or preoperative evaluation/ or preoperative treatment/))

182 or/174-181 [\*\*\*\*Confusion, delirium terms\*\*\*\*]

183 173 and 182 [\*\*\*\*Base clinical set\*\*\*\*]

## Appendix 9. Study Screening Form

Reviewer Initials <input type="text"/>	Review Date: <input type="text"/> / <input type="text"/> / <input type="text"/> (dd/mm/yy)	
Primary Author		
Citation (title, journal, year, vol, pg)		
Level of Review	<input type="checkbox"/> Title and Abstract	<input type="checkbox"/> Full text
<b>STUDY SELECTION</b>		
Study Type	RCT or quasi-randomised trial	<input type="checkbox"/> Yes <input type="checkbox"/> No
Population	Patient with, or deemed at high risk of delirium, assessed with a validated delirium screening tool or via psychiatric assessment (e.g. DSM-IV)	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Study patients received care in an acute care setting/hospital	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Study does not have alcohol or benzodiazepine withdrawal as the sole reason for study inclusion (i.e. focus of study cannot be management of delirium secondary to drug/alcohol withdrawal)	<input type="checkbox"/> Yes <input type="checkbox"/> No
Intervention	Antipsychotic drug for treatment of delirium	<input type="checkbox"/> Yes <input type="checkbox"/> No
Comparison	Placebo, alternative drug class, or other antipsychotic	<input type="checkbox"/> Yes <input type="checkbox"/> No
<b>Decision</b>	<input type="checkbox"/> INCLUDE <input type="checkbox"/> EXCLUDE	
Primary reason for exclusion	<input type="checkbox"/> Study type	
	<input type="checkbox"/> Population	
	<input type="checkbox"/> Intervention	
	<input type="checkbox"/> Comparison	

## WHAT'S NEW

Last assessed as up-to-date: 20 July 2017.

Date	Event	Description
20 July 2017	New citation required and conclusions have changed	New studies added and content extensively revised. Conclusions changed. Changes to author team and new lead author
20 July 2017	New search has been performed	Top-up searches were performed for this review in May 2011, July 2013, October 2015, November 2016 and July 20 2017. New studies were identified for inclusion in the review

## HISTORY

Protocol first published: Issue 1, 2006

Review first published: Issue 2, 2007

Date	Event	Description
23 October 2008	Amended	Converted to new review format.
2 February 2007	New citation required and conclusions have changed	Substantive amendment

## CONTRIBUTIONS OF AUTHORS

LB and LR reviewed the search results.

SM, MMP, JSL, and CB extracted data for included studies.

LB, BH and DAF completed the analysis and generated the 'Summary of Findings' table and GRADE Evidence.

LB generated the first draft of the review.

NS acted as an independent arbiter for study exclusion, and verified 'risk of bias' assessments.

All authors interpreted the analysis and contributed to the write-up of the review.

## DECLARATIONS OF INTEREST

None known.



## SOURCES OF SUPPORT

### Internal sources

- Department of Pharmacy, Mount Sinai Hospital, Toronto, Canada.

### External sources

- Canadian Frailty Network (Previously known as Technology Evaluation in the Elderly Network [TVN] ([www.tvn-nce.ca](http://www.tvn-nce.ca))), Canada.  
Funded by the Government of Canada through the Networks of Centres of Excellence (NCE), Technology Evaluation in the Elderly facilitates evidence-based research, knowledge sharing and clinical practices that improve healthcare outcomes for frail elderly Canadians, their families and caregivers.
- NIHR, UK.  
This update was supported by the National Institute for Health Research (NIHR), via Cochrane Infrastructure funding to the Cochrane Dementia and Cognitive Improvement group. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, National Health Service or the Department of Health

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- The original protocol has been modified to exclude critically ill patients as this population overlaps with the Cochrane Anaesthesia, Critical and Emergency Care Group's Protocol ACE311.
- Antipsychotics are the most commonly prescribed class of drug for the treatment of delirium in hospitalised patients. We felt it necessary to refine the original protocol's research question 'to compare the efficacy and incidence of adverse effects of haloperidol with risperidone, olanzapine, and quetiapine in the treatment of delirium' to instead explore the effects of antipsychotics versus alternative (i.e. nonantipsychotic drugs) or placebo on outcomes of hospitalised patients with delirium. We made the original primary question a secondary question.
- We included Health-related quality of life as an outcome and expanded upon the adverse events that we sought from the trials.
- The 'Summary of findings' table was generated in accordance with current Cochrane Collaboration Guidance utilising GRADE assessments.
- Authorship for this update has been changed to include new members and remove those no longer involved in the review.

## INDEX TERMS

### Medical Subject Headings (MeSH)

Antipsychotic Agents [adverse effects; \*therapeutic use]; Benzodiazepines [adverse effects; therapeutic use]; Delirium [\*drug therapy]; Haloperidol [adverse effects; therapeutic use]; Randomized Controlled Trials as Topic; Risperidone [adverse effects; therapeutic use]

## **MeSH check words**

Adult; Female; Humans; Male